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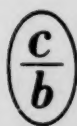
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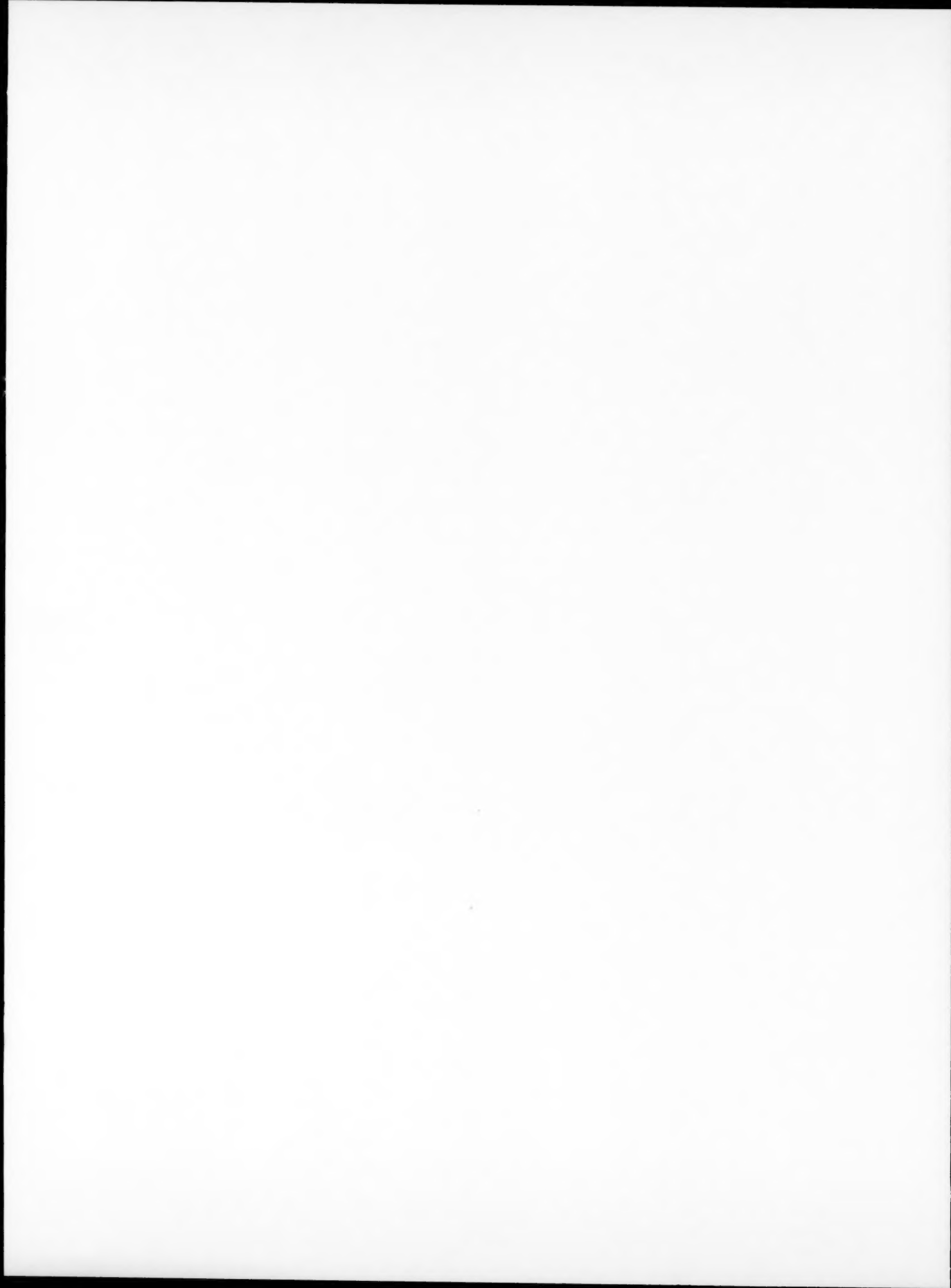
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CATALYTIC VAPOR PHASE KETONE FORMATION FROM ACETIC ACID OVER MAGNESIUM, ZINC, AND CADMIUM OXIDES

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Previously [1, 2] we considered possible mechanisms for the reaction of ketone formation from carboxylic acids and gave thermodynamic calculations for this process when it occurred with intermediate formation of acetate, and we discussed some characteristics of the decomposition of Ca, Sr, and Mg acetates. We showed that the ionic or radical mechanisms of the reaction were not essential, and in some cases were certainly incorrect. In an analysis of the experimental data we suggested the idea of formation of an intermediate active six-membered molecular complex.

The purpose of the present work is to obtain data on the kinetics of ketone formation from CH_3COOH over oxides of Mg, Zn, and Cd and to explain the mechanism of the ketone forming reaction over a wide range of temperatures.

EXPERIMENTAL

Preparation of the catalysts. ZnO was obtained by precipitation from a solution of $\text{Zn}(\text{NO}_3)_2$ with 25% NH_3 [3]; the precipitate was filtered, washed to a negative reaction for NO_3 with diphenylamine, pressed out, formed into tablets $2 \times 2 \text{ mm}^2$, dried at 100° , and ignited in a stream of nitrogen at $500\text{--}600^\circ$. The final weight of the catalyst was 0.46 g/cm^3 .

CdO was obtained by precipitation from a solution of $\text{Cd}(\text{NO}_3)_2$ with ammonium carbonate [3]; the precipitate was washed, pressed, formed into tablets $2 \times 2 \text{ mm}^2$, and ignited at 600° , first in a stream of air and then in a stream of nitrogen after which it was sealed into ampules. The weight of CdO was 1.1 g/cm^3 .

MgO was obtained from previously synthesized magnesium carbonate [1] by ignition at 550° in a stream of nitrogen. The weight of MgO was 0.125 g/cm^3 .

EXPERIMENTAL METHODS

For carrying out the reaction of ketone formation a quartz tube with 4 cm^3 of catalyst was placed in a horizontal furnace heated to a determined constant temperature and regulated by an electric relay with an accuracy of $\pm 0.5^\circ$. Before the experiment, the system was blown out with nitrogen. The acetic acid was supplied from an automatic deliverer [4]. After the experiment had been carried out, the tube with the catalyst was removed from the furnace, cooled by blowing a stream of nitrogen through it, and the catalyst was studied by the x-ray powder method*.

*Phase analysis of the samples was carried out with the participation of L. D. Kretalova, to whom the authors express their thanks.

The x-ray patterns of the MgO and CdO preparations were taken with an RKD camera with illumination by the K_{α} series of copper with a nickel filter: at 35 kv and 10 ma the exposure for MgO was 8-12 hours and for CdO 3-3.5 hours. The ZnO preparations were photographed in an RPK-2 camera with iron illumination and a manganese filter; at 14 ma and 34 kv the exposure was 10 hours. Identification of the phase was carried out from data in the tables [5] and also by comparing the x-ray patterns of the working and starting catalysts with the x-ray patterns of the corresponding acetates. The accuracy of the x-ray pattern measurements averaged 0.2 mm. All the preparations studied were crystalline; however, the x-ray patterns of the acetates and the preparations which contained acetates differed in the strong background and diffuse lines because of the very high dispersity or considerable content of amorphous phase.

The analysis of the gaseous products collected in the eudiometer was carried out in a VTI-1 apparatus.

Thermogravimetric study of the decomposition of the Cd and Zn acetates (c. p.) and also of the catalysts after they had been used was carried out on the apparatus described before [2]. The samples weighed 160-260 mg, the rise in temperature was carried out at a rate of 1°/min, and in some special experiments the temperature at the same rate was brought to a definite value and then maintained approximately constant.

To determine whether there was reduction to the metal, we measured the magnetic susceptibility of the CdO preparation at 20° by the method of Faraday [6]*.

EXPERIMENTAL DATA

In Figs. 1 and 2 we give the thermogravimetric curves for decomposition of the dihydrate and anhydrous forms of Zn acetate. The temperature is on the abscissa and the loss in weight (in mg) on the ordinate.

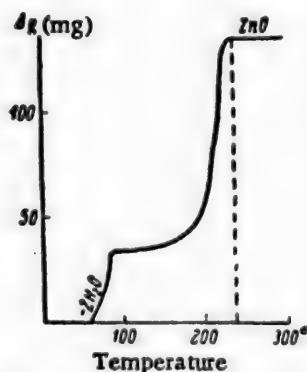


Fig. 1. Decomposition of $Zn(CH_3COO)_2 \cdot 2H_2O$ (sample 210 mg).

Fig. 1 shows that loss of water is complete at 100°. Decomposition of Zn acetate begins and ends below the melting point (242°) [7], which contradicts the data of [8]. The experiments showed that if the temperature is brought to about 180° and then kept constant, the zinc acetate dihydrate is completely decomposed with the formation of ZnO. Anhydrous zinc acetate, dried at 160°, also begins to decompose below 200°, and if the temperature is kept about constant, even at 205° it is completely decomposed (Fig. 2).

Decomposition of cadmium acetate dihydrate (Fig. 3) also occurred somewhat differently from the description in [8]. At first, up to 100°, there was loss of 1.5 molecules of water, and then to 200° of the remaining 0.5 molecule of water. Actual decomposition of cadmium acetate began at about 210° and ended at 300°.

Based on the temperature of beginning decomposition of acetates of Mg [2], Zn, and Cd, we studied the kinetics of vapor phase catalytic ketone formation from CH_3COOH over the oxides of these metals.

The results of measurement of the catalytic activity are given graphically in Fig. 4: on the abscissa is the temperature, on the ordinate the activity a expressed in ml CO_2 (standard conditions) formed in ketone formation from 1 ml of CH_3COOH (complete transformation of 1 ml of CH_3COOH into CH_3COCH_3 formed 196 ml of CO_2). For comparison we have also added to the graph the results of experiments on ketone formation from acetic acid over the carbonates of Mg, Ca, Sr, and Ba [1]. The activities of MgO, ZnO, and CdO at experimental temperatures close to the decomposition temperatures of the corresponding acetates are zero. In no case did we succeed in dropping below the temperature of decomposition of the acetate. At temperatures of ketone formation close to the decomposition temperatures of the acetates, the catalyst sharply changed its external form, and its density increased several fold. Thus, in the case of CdO (240-250°) the catalyst grew lighter in color and its density increased 2.5 times. Acetic acid first reacted with the catalyst to form the acetate and then distilled without change. A similar effect was also observed by Senderens [9].

*These measurements were made in our laboratory by A. A. Slinkin.

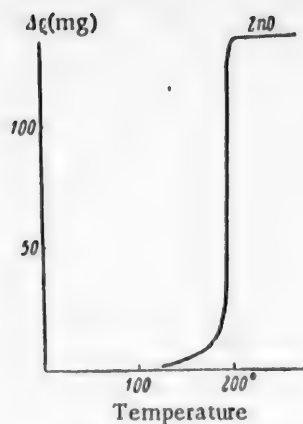


Fig. 2. Decomposition of $\text{Zn} \cdot (\text{CH}_3\text{COO})_2$ dried at 160° (sample 261 mg, temperature after reaching 200° is kept constant).

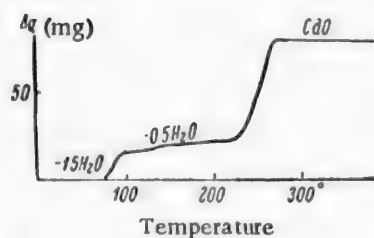


Fig. 3. Decomposition of $\text{Cd} \cdot (\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ (sample 160 mg).

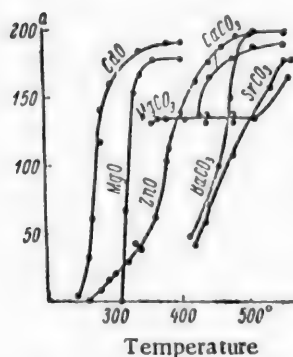
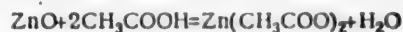


Fig. 4. Change of catalytic activity with temperature (a-milliliters CO_2 per 1 ml CH_3COOH).

The results of the phase analysis are shown schematically in Fig. 5, where the intensity of the lines is on the ordinate and the values (in Å) for the interface distances are on the abscissa. The x-ray patterns for the initial and working catalysts differ greatly from each other. At $240\text{--}270^\circ$ the x-ray pattern of the CdO preparation (Fig. 5a) shows lines of the oxide, carbonate, and acetate of cadmium. From 300° and over we see only the line of CdO . The MgO preparation up to 330° shows along with the MgO lines also the lines of the acetate and probably the carbonate (Fig. 5b). Since because of the strong background we could not photograph the MgO preparation in the iron illumination, which gives more lines, but only with copper the basic lines for Mg acetate were concentrated in a region of small angle, which lessened the accuracy of the calculation. Therefore we obtained the thermogravimetric curve for the decomposition of the working MgO catalyst (Fig. 6) which was compared with the analogous curve for the decomposition of magnesium acetate [2]. The decomposition of magnesium carbonate begins at a lower temperature than the decomposition temperature of the working catalyst and the acetate. While the decompositions of the working catalyst and the acetate occur continuously, the decomposition of the carbonate is stepwise, which is evidently connected with the stability of the phase $x\text{MgO} \cdot y\text{CO}_2$ [10]. At a temperature of about 390° decomposition of the acetate and the spent catalyst is nearly complete, but at this temperature the carbonate is only half decomposed. If from the amount of MgO obtained after decomposition of a sample of spent catalyst we calculate the amount of carbonate or acetate from which the MgO was formed, then for the carbonate we obtain lower and for the acetate, higher values. Evidently the spent catalyst consists chiefly of MgO and acetate with an admixture of a small amount of magnesium carbonate.

Catalytic ketone formation from CH_3COOH over ZnO up to and including 350° occurs with formation of a white deposit in the cold part of the tube: as the deposit increases, the amount of catalyst lessens. It was noted that as the amount of catalyst decreased, its activity did not change, and when the remainder of the catalyst was very slight, it fell sharply. X-ray analysis of the deposit (Fig. 5c) showed only the lines of zinc acetate. However, it is known that zinc acetate is nonvolatile and is incapable of subliming, in distinction from the basic acetate $\text{Zn}_4\text{O}(\text{CH}_3\text{COO})_6$ [11-14]. According to data published previously the formation and sublimation of $\text{Zn}_4\text{O}(\text{CH}_3\text{COO})_6$ occur in a vacuum. Our experiments showed that this process also occurs at atmospheric pressure and, there, is markedly shifted

toward formation of the basic acetate. The thermogravimetric curve of decomposition of the white deposit (Fig. 7) shows full agreement with the analogous curves for zinc acetate (Figs. 1, 2) and the stoichiometric reaction agrees well with the decomposition of simple and not basic zinc acetate. Evidently zinc acetate is first formed



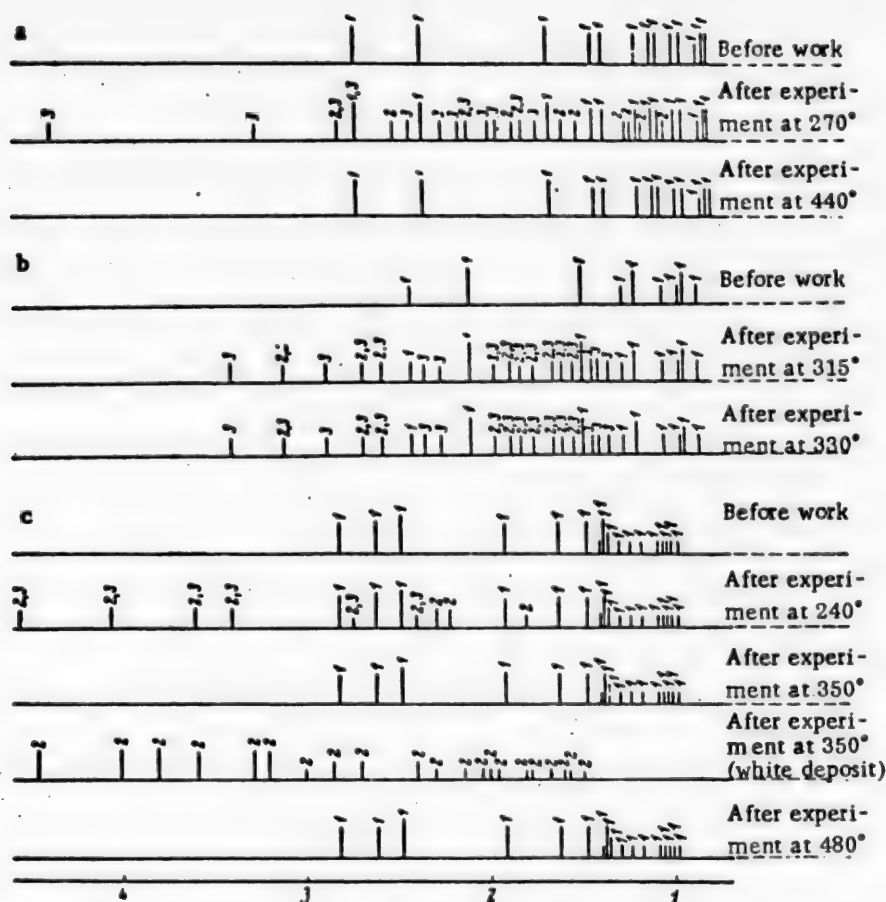


Fig. 5. Results of x-ray analysis of the catalysts. a) Cadmium, b) magnesium, c) zinc. Designations of phase: 1) Metal oxide; 2) metal carbonate; 3) metal acetate.

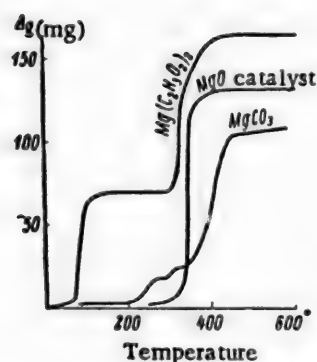


Fig. 6. Decomposition of MgCO_3 , $\text{Mg}(\text{C}_2\text{H}_3\text{O}_2)_2$ and the MgO catalyst after work (ketone formation from CH_3COOH at 310°).

after experiments at 440° it is -0.27 , and for metallic cadmium it is -0.1746 [15]). After heating in air at 550° for 8 hours the susceptibility of the catalyst which worked at 440° returns to its former value and the color changes

and in the presence of water this splits out part of its acetic acid and is converted to the basic acetate



The basic zinc acetate sublimates and decomposes with formation of acetate and oxide on the walls of the quartz tube



We note that at 240° no deposit is found. This agrees well with the fact that sublimation of the basic acetate occurs at 270 – 280° [14].

The composition of the gaseous products indicates that on MgO ketone formation occurs without side reactions, on ZnO almost the same (1–2% unsaturated hydrocarbons), on CdO up to 400° without side reactions (2.5% unsaturated hydrocarbons), and at 440° there is an oxidation-reduction type of process: the amount of H_2 , CO and saturated hydrocarbons reaches 5.5%, the color of the spent catalyst changes to green, and measurement of the magnetic susceptibility shows the formation of metallic cadmium ($\chi \cdot 10^6$ for CdO before work and after experiments at 260 – 360° is -0.33 ;

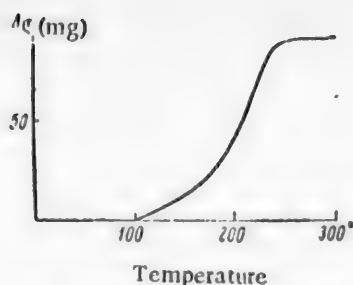


Fig. 7. Decomposition of the white deposit obtained in ketone formation from CH_3COOH over ZnO at 320° (weight 162 mg).

from green to the red characteristic of CdO . Calculation by the law of additivity shows that about 10% of the catalyst consists of metallic cadmium. Attempts at thermogravimetric determination of the overweight due to oxidation of the Cd , as would be expected, did not succeed, since at a weight of 150 mg the overweight would only be 1.5 mg. The absence of change in magnetic susceptibility of catalysts which contain acetate is explained by the small difference between the values of the susceptibility of cadmium acetate and oxide.

DISCUSSION OF RESULTS

Our experiments showed that with MgO , CdO , and ZnO the formation of ketone from CH_3COOH occurs in a way analogous to that with the carbonates of Mg , Ca , Sr , and Ba , that is, by inter-

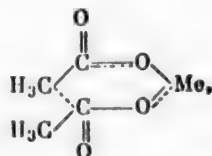
mediate formation of the acetates of the corresponding metals. In no case of ketone formation was the temperature lower than the decomposition temperature of the corresponding acetate. Phase analysis of MgO , CdO , and ZnO catalysts after running ketone formation up to 350° showed the presence of acetates of the metals making up the phase volume. Thus, in the case also of the catalysts described here at the temperature measured, intermediate compounds are formed in the entire volume of the catalyst. At high temperatures the rate of decomposition of the acetates becomes greater and therefore they are no longer found in the working catalysts. At temperatures near the decomposition temperatures of the acetates the rate of their formation considerably surpasses the rate of their decomposition, and the catalyst is completely converted into the acetate.

Ketone formation on ZnO is complicated by the formation of the volatile basic zinc acetate which decomposes on the tube walls, and therefore in the kinetics of the decomposition of zinc acetate there should be a diffusion effect.

The activation energy E of ketone formation from CH_3COOH was calculated graphically for the experiments in which conversion of CH_3COOH into CH_3COCH_3 did not exceed 30%. MgO was excluded because of the comparatively high temperature of decomposition of the acetate, whose splitting limited the beginning of the reaction, and the great temperature coefficient of the reaction. The values for the activation energy for the different catalysts, including also the alkaline earth carbonates, are given below along with other data.

It is advisable to compare the activation energies of ketone formation by the different oxides, though the value of E obtained for ZnO is low for the reason given above, and also corresponding to the data of [16] which show that E for decomposition of the acetate is 45 kcal/mole. Since we showed in our experiments that acetate is the intermediate product, and since the step of decomposition of the acetate determines the rate of the reaction, E for ketone formation from CH_3COOH on ZnO should be equal to about 45 kcal/mole which is approximately equal to E for CdO .

According to the values of E we can divide the catalysts into two groups: $\text{CaCO}_3 < \text{SrCO}_3 < \text{BaCO}_3$, and ZnO , $\text{CdO} < \text{MgO}$. In both groups E rises with strengthening of the basic properties of the catalyst. This confirms the idea expressed in the previous work [1] that the highest activation barrier is connected with the reaction of decomposition and not with the formation of acetate. In the active six-membered complex [17], which was assigned the structure



depending on the covalent bond $\text{Me}-\text{O}$, electrons will be drawn off by the oxygen of the carbonyl group $\text{C}=\text{O}$ either from the $\text{Me}-\text{O}$ bond or from another bond, especially from the $\text{C}-\text{H}$ of the methyl group [18]. With increased covalency of the $\text{Me}-\text{O}$ bond the electrons of the methyl group will be attached more strongly and this will create a positive charge on the hydrogen and a negative charge on the carbon. At the same time the attraction of the electrons to the oxygen of the carbonyl group will permit formation of a

positive charge on the carbon. Such electron shifts will permit formation of bonds $\text{H}_3\text{C}\cdots\overset{\cdot}{\text{C}}=\text{O}$, which will cause a lowering of the activation energy of the reaction. Thus, increase in the covalency of the Me-O bond lowers the activation energy. The degree of the covalency of the Me-O bond can be judged by the difference in electronegativity (X) of the atoms of oxygen and metal. Then the degree of ionic character of the bond A-B (in %) (ICB) and hence also the degree of covalency of the bond (in %) (DCB) can be determined by the Pauling equation [19]:

$$\text{ICB} = 1 - e^{-\frac{1}{4}(X_A - X_B)^2}$$

The data on relative electronegativities, taken from [20], are given with other data in Table 1.

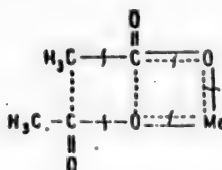
TABLE 1

Element	X	$X_0 - X_{\text{Me}}$	ICB (%)	DCB (%)
Mg	1.12	2.42	77.42	22.58
Ca	0.985	2.555	80.45	19.55
Sr	0.928	2.612	81.85	18.15
Ba	0.903	2.637	82.40	17.60
Zn	1.464	2.076	65.93	34.07
Cd	1.396	2.144	68.30	31.70
O	3.54	—	—	—

TABLE 2

	Zn	Cd	Mg	Ca	Sr	Ba
q (kcal/mole) [21, 22]	17	21.8	—	42.5	55.7	61.0
DCB (%)	34.07	31.70	22.58	19.55	18.15	17.60
E by MeO	11 (45*)	36.6	114	48.2	71.8	81.4
E by MeCO_3	28**	40	—	27.6	34.5	39.9
Log A	5.3	9.2	36	4.3	4.9	6.4

If we compare the values of E (Table 2) for carbonates of Ca, Sr, and Ba, and for oxides of Mg and Cd, we can see that the activation energy of ketone formation by carbonates is somewhat lower. This is connected with the fact that when the splitting of the six-membered transitional complex leads to the formation of carbonate, as occurs in the case of the complex of alkaline earth metals, there is a further rearrangement of the bonds, passing through the formation of a four-membered complex.



The gain due to energy of combination in the four-membered complex can be estimated approximately from the heat effect q of formation of carbonate from the metal oxide and CO_2 : $\text{MeO} + \text{CO}_2 = \text{MeCO}_3 + q$. Such a rearrangement of bonds in the case of formation of the carbonate has an isoenergetic character (rupture of

*Energy of activation of decomposition of zinc acetate [16].

**Energy of activation of ketone formation from CH_3COOH by ZnCO_3 , calculated on the assumption that the energy of activation of ketone formation by ZnO is equal to the energy of activation of decomposition of zinc acetate (45 kcal/mole).

the bonds σ C-C, σ Me-O, π Me-O, π C-O, and formation of the bonds σ C-C, π Me-O, π C-O, σ Me-O, σ C-O). Thus from the point of view of energy this process is favorable and leads to the greatest lowering of E [17]. In the case of formation of metal oxides, such an isoenergetic rearrangement of the bonds does not occur: there is rupture of the bonds σ C-C, σ Me-O, σ C-O and formation of bonds σ C-C, π Me-O, π C-O.

It is of interest to calculate E of ketone formation by the oxides of the alkaline earth metals, and also by the carbonates of zinc and cadmium, since experimental determinations of these values is impossible (under the experimental conditions the oxides of the alkaline earth metals are converted to carbonates, and further ketone formation occurs on the metal carbonates, and the carbonates of Zn and Cd are decomposed below the temperature of ketone formation). Corresponding with the above mentioned energy of activation by MeO, the energy of activation by MeCO₃ is the same plus the heat effect of the reaction.

The data of Table 2 show that for the calculated values of activation energy the same order of succession is retained with increasing basic properties of the metal. Comparison of the DCB (%) with the calculated and experimental determinations of the activation energy of ketone formation confirms the idea of the effect of covalency of the bond of MeO on the activation energy of the reaction.

The supplementary formation of the four membered complex leads to a "twisted" molecule and to a sharp decrease in "A" which is found in the experiment (Table 2). Ketone formation from CH₃COOH by the carbonates of Ca, Sr, and Ba is characterized by a much lower lg A than by oxides of Cd and Mg. The low value of lg A in the reaction of ketone formation by ZnO is evidently connected with the diffusion process of transfer of substance and formation of the basic acetate Zn₄(CH₃COO)₆.

We can assume that increase in E in the series CaCO₃ < SrCO₃ < BaCO₃ is explained by increase in expenditure of energy in transfer from the crystal lattice of carbonate to the acetate lattice. The calculations of K. B. Yatsimirskii [23] permit us to estimate the difference in energy of the crystal lattice U_{MeCO₃} and U_{Me(CH₃COO)₂}: for calcium, $\Delta U = 722 - 581 = 141$ kcal/mole; for strontium, $\Delta U = 675 - 545 = 130$ kcal/mole; for barium, $\Delta U = 647 - 521 = 126$ kcal/mole; that is, the expenditure of energy decreases in the series Ca, Sr, Ba, which contradicts the direction of change of E. Comparison of E and lg A of ketone formation by different catalysts permits us to establish a sharply expressed compensation effect [24] in which the growth of E is accompanied by a growth of lg A. In a number of cases the reaction of ketone formation is accompanied by side reactions whose intensity depends on the nature of the catalyst. This occurs either at high temperatures (>500°) [1], or when the value of E is very great. We can properly say that with good ketone formation catalysts, there cannot be catalysts with a large E (about 60 kcal/mole). In fact, study of the thermal decomposition of CH₃COOH at 500-900° [25] showed that ketenic (CH₃COOH → CH₂=C=O + H₂O) and methane (CH₃COOH → CH₄ + CO₂) decompositions are characterized by E equal to 67.5 and 62 kcal/mole respectively. It is evident that at E of ketone formation on this order or over, the reaction of pyrolysis of CH₃COOH will complete successfully with ketone formation. Thus, for example, on CdO at 440° the reaction of ketone formation is accompanied by side processes which lead to reduction of part of the catalyst to metallic Cd. In the case of the reaction of ketone formation itself, in accord with the temperature coefficient, the equilibrium is reached on MgO and CdO at 350° (89.5 and 97.2% transformation respectively), while on ZnO it is reached only at 480°.

SUMMARY

1. Vapor phase catalytic ketone formation from CH₃COOH was studied in a flowing system at 240-500° over MgO, ZnO and CdO. It was found that the reaction of ketone formation does not occur at temperatures below the temperature of decomposition of the acetates of Mg, Zn, and Cd. Formation of the acetate in the process of ketone formation was confirmed by x-ray and thermogravimetric methods. Calculation of the activation energy and exponent A for the reaction of ketone formation was carried out for the oxides mentioned.

2. It was shown that with increased basicity of the oxides or carbonates both the energy of activation and the exponent A of the reaction increased. The value for the activation energy for the reaction of the oxides of the alkaline earth metals and the carbonates of Zn and Cd was estimated on the basis of theoretical ideas.

3. The formation of an active intermediate four membered complex was suggested and on this idea the difference in activation energy between oxides and carbonates was explained. A connection was shown between the covalency of the Me-O bond in the intermediate complex and the activation energy of the ketone formation process.

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EQUILIBRIUM OF THREE LIQUID PHASES IN A FOUR COMPONENT
SYSTEM INCLUDING A PREDOMINANT SYSTEM
WITH A CHEMICAL COMPOUND

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From the point of view of the theory of predominance at the interface between the phases the composition should reflect preferably the interaction of the components of the predominant binary system. This idea is experimentally confirmed in a study of the state of the interface of a two phase liquid in a three component system. Hence it can be assumed that this is also correct for the surfaces in a three phase state in a four component system which consists of one predominant binary system.

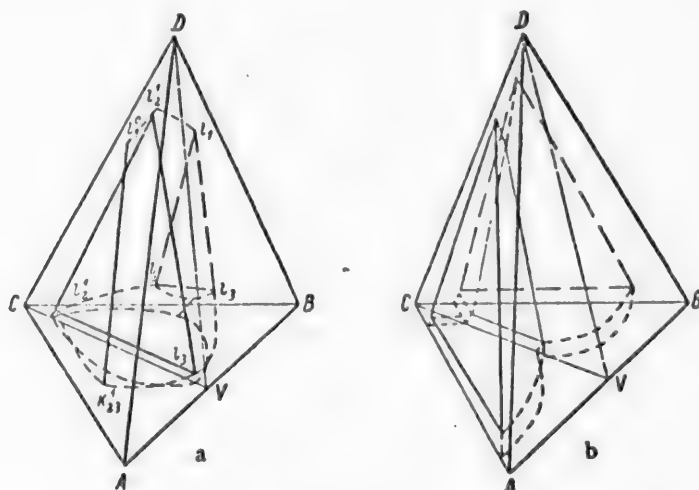


Fig. 1. Two cases of the diagram of state of the system (explanation in text).

We have studied this question for the case in which the predominant system includes a chemical compound.

First we consider the question theoretically.

We can assume at least two cases of the diagram of state for the system which we are discussing, connected with the relative reciprocal solubilities of the phases in the three phase state, at a quasi-ternary section of the tetrahedron, and in the two bounding ternary systems which comprise this state. One of these should reflect the minimum and the other the maximum reciprocal solubility. Figs. 1a and 1b illustrate these. In the first case the three phase state in the form of a critical node, with corresponding change in temperature, first arises on the planes ACD and BCD (in Fig. 1a one of these is shown). In the second case, on the other hand, the critical node first arises on the quasi-ternary section CVD (Fig. 1b).

Corresponding to this there will also be found the diagram of release from the three phase state on the section of the tetrahedron passing through line CD, and the different points on line AB which correspond to the predominant system (they are shown in Fig. 2 a and 2 b), and also the sections of the tetrahedron parallel to plane ABC. The latter are given in Figs. 3 a and 3 b.

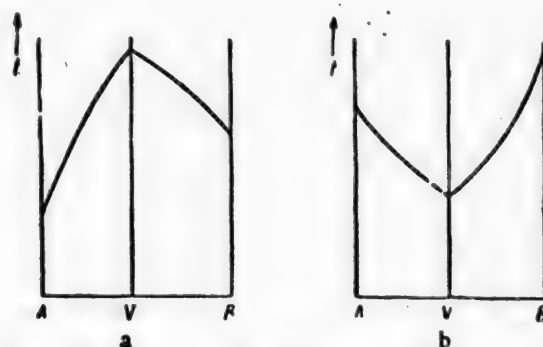


Fig. 2. Extremes in the temperature diagrams corresponding to the chemical compound.

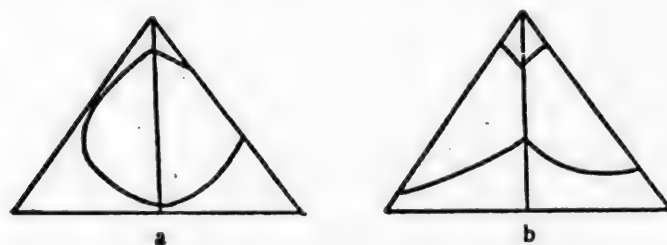


Fig. 3. Extreme points on the curves of isothermal sections.

As is evident, on the temperature diagrams the presence of a chemical compound should be shown by extremes (maxima or minima), and on the isothermal sections by extreme points on the curves which map out the field of the three phase state.

We observe that such equilibria are met in practice in different variations of these cases which depend on the absence of a three phase state on the quasi-ternary section in the first of them, and the absence of this state in one or even both ternary bounding systems in the second.

Experimentally we have studied the equilibrium of three liquid phases in the four component system sulfur-water-phenol-pyridine.

EXPERIMENTAL

All four ternary bounding systems have equilibrium regions of two liquid phases. Of these only one ternary system, water-sulfur-phenol, has an equilibrium region of three liquid phases [1]. The predominant binary system is the phenol-pyridine system.

The polythermal method of Alekseev was used to study the equilibrium of the three liquid phases for the section of the polyhedron with composition answering to 20 weight % sulfur in its section running through the line water-sulfur and a series of points on the line phenol-pyridine with ratios of the latter (by weight): 9:1, 4:1, 7:3, 5.5:4.5, 4.5:5.5, and 3:7. In the study we observed the temperature of transformation of the two phase state of the complex taken to the three phase. The experimental data are given in the table and expressed graphically in Fig. 4. For each polytherm of one or another section we determined from its graph the maximum temperature of formation of three liquid phases. On the basis of these data we constructed the functional curve of

dependence of maximum temperature of formation of three liquid phases on the state of the binary predominant system (Fig. 5). The polythermal curve sections were used to construct the isotherms corresponding to 115, 130, 140, and 145°. The isotherms are shown graphically in Fig. 6.

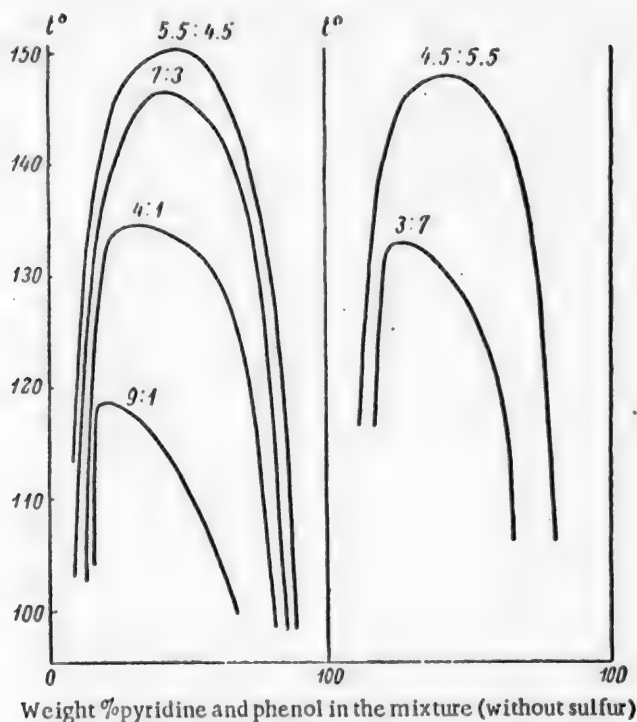


Fig. 4. Polythermal sections of the system water-sulfur-phenol-pyridine.

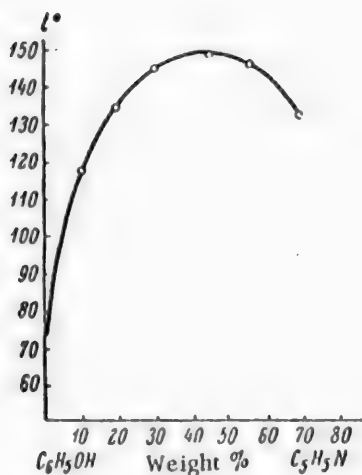


Fig. 5. Dependence of maximum temperature of formation of three liquid phases on composition of binary predominant system.

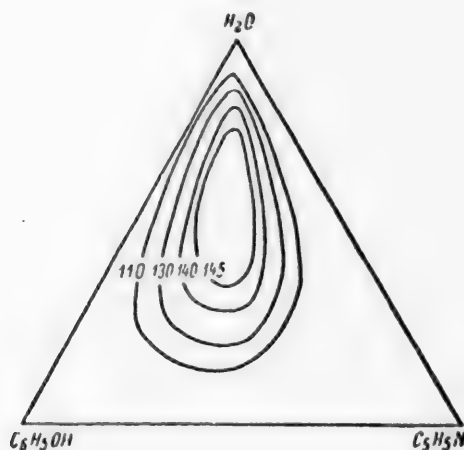


Fig. 6. Isotherms of equilibrium of three liquid phases in the mixture water-sulfur-phenol-pyridine which contains 20 weight % sulfur.

Equilibrium of Three Liquid Phases in the Four Component System Pyridine-Phenol-Water-Sulfur (Section 20 Weight % Sulfur)

Wt. ratio phenol: pyridine	Wt. % pyri- dine and phe- nol in mix- ture (no S)	Wt. % pyri- dine in mix- ture (without S and H ₂ O)	Conversion temp. from two phase to three phase state	Wt. ratio phenol: pyridine	Wt. % pyri- dine and phe- nol in mix- ture (no S)	Wt. % pyri- dine in mix- ture (without S and H ₂ O)	Conversion temp. from two phase to three phase state
9:1	17.4	10.0	110.0°	5.5:4.5	10.0	45.0	114.0
	20.1		118.0		20.0		143.0
	28.7		117.0		29.6		148.0*
	40.0		114.5-115*		39.3		149.5
	50.0		111.0		49.8		149.0
	58.0		106.0		60.3		147.0
	70.0		92.5		70.0		141.0
4:1	15.0	20.0	115.0	4.5:5.5	89.0	55.0	129.0
	20.0		130.0*		89.0		80.0
	30.0		134.0		14.0		125.0
	40.0		133.0		20.0		140.0
	50.0		132.0		30.0		146.0
	60.0		130.0		40.0		146.0
	70.0		121.0		50.0		146.5
7:3	80.0	30.0	100.0	3:7	59.6	70.0	144.0
	15.0		129.0		69.6		139.0
	19.6		137.0*		80.0		119.5
	29.5		144.0		19.8		126.0
	39.8		146.0		30.0		132.0
	48.0		145.0		37.8		131.0
	59.1		143.0		50.0		127.5
	70.0		136.0		59.8		122.0
	80.0		118.5				
	85.0		106.0				

* Critical opalescence.

DISCUSSION OF RESULTS

From the experimental data which we obtained and the graphs which we constructed on this basis it can be clearly seen that our ideas are fully confirmed. The curve of temperature of formation of the three liquid phases has a maximum (149°) which corresponds to the section passing through a composition of the chemical compound between $C_6H_5OH \cdot C_5H_5N$ (54.3 weight % phenol). This extreme is much higher than the temperature of formation of three liquid phases in the ternary system water-sulfur-phenol (71°). All the isotherms at temperatures above 71° have the characteristic form of closed concentric curves drawn on the section water-phenol-pyridine and are analogous to the isotherms of the two phase state of the three component system water-phenol-pyridine.

We note that the temperature of formation of the three liquid phases in the section (149°) corresponding to a chemical compound of the above mentioned composition exceeds the temperature of formation of two liquid phases (144°) in the quasi-binary section of the ternary system water-phenol-pyridine. This shows that in the beginning, with fall in temperature the three phase state, in the form of a critical node with a critical point turned to the plane of the ternary system water-phenol-pyridine, is found in the tetrahedron on its quasi-ternary section at a temperature at which there is still no formation of two liquid phases in the quasi-binary section.

SUMMARY

1. We have studied the spacial contour of the three liquid phases in the section with 20 weight % sulfur for the four component system water-phenol-pyridine-sulfur at a number of temperatures. We have shown reflected here the reaction of the components of the binary predominant system phenol-pyridine.

2. We have shown the corresponding ability to form three liquid phases in the ternary system and in the quasi-ternary section of the four component system for the case where the temperature curve of formation of the three liquid phases has a maximum.

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A STUDY OF SOLUBILITY IN THE SYSTEM LITHIUM CITRATE - AMMONIUM CITRATE - WATER

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Citrates, which are present in small amounts in the soil, have an important physicochemical role in stabilizing the colloidal particles of mineral and organic origin in the soil. This improves the absorptive power of the soil, which depends chiefly on its content of colloidal particles of organo-mineral origin. It is known that the finest colloidal particles are the most valuable for nutrition, since the substances needed for plants are most easily dissolved from them by water. On the basis of these considerations we have proposed a series of investigations on reciprocal solubilities in an aqueous medium of lithium, ammonium, potassium and calcium citrates, that is, those substances which play an important part in the growth of plants. Judging from the literature data, this is the first study of the problem.

EXPERIMENTAL

As starting substances we used C. P. salts. The study was carried out by the visual polythermal method on the appearance of the first crystals of ice, since the crystallization of the other components could not be observed due to formation of amorphous mixtures. Hysteresis between the appearance of the first crystals and the disappearance of the last was observed within the limits 0.1-0.2°. The observations were made in glass tubes with a glass stirrer and thermometer with an accuracy to 0.1°. During the study we noted that lithium and ammonium citrates gave amorphous viscous masses in whose composition there evidently occurred solid solutions of the type $mC_6H_7O_7Li \cdot nC_6H_7O_7NH_4$.

We studied the system from the moment of appearance of the amorphous mass to full freezing of the system. In all we studied six sections, starting from the point corresponding to water.

In order to shorten the report, the numerical data and figures for the inner sections, which are not characteristic, have been omitted. The eutectic of the system $C_6H_7O_7Li-H_2O$ contains 35.5% $C_6H_7O_7Li$ and has a m. p. -11.5°; the eutectic for the system $C_6H_7O_7NH_4-H_2O$ contains 46% $C_6H_7O_7NH_4$ and melts at -6.2°.

On the basis of these results we have constructed the diagram of state for the system, which shows the fields of crystallization of water and the solid solutions which we have established for the two citrates (figure).

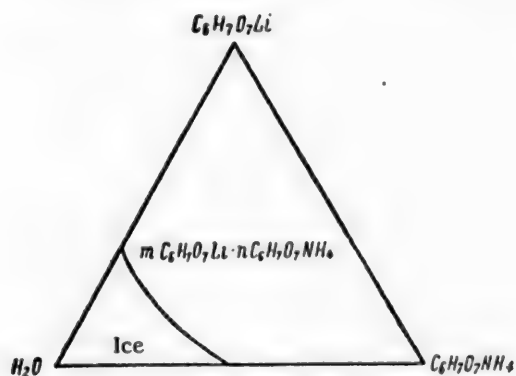


Diagram of state for the ternary system $C_6H_7O_7Li-C_6H_7O_7NH_4-H_2O$.

SUMMARY

We have studied the system $\text{C}_6\text{H}_7\text{O}_7\text{Li}-\text{C}_6\text{H}_7\text{O}_7\text{NH}_4-\text{H}_2\text{O}$ from 0° to complete freezing. We find in the system the formation of solid solutions.

THE SOLVATION OF THE FERRICENIUM ION

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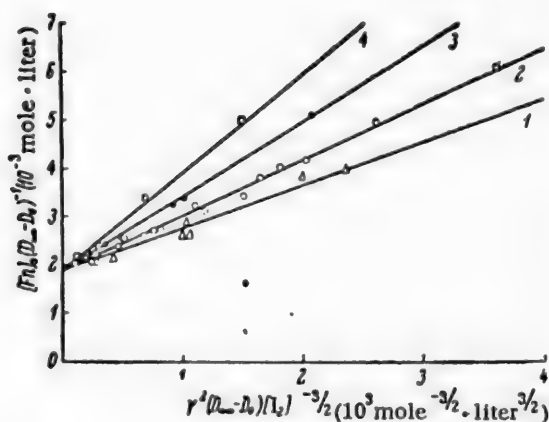
pp. 3167-3171, October, 1960

Original article submitted December 7, 1959

In a previous communication [1] on the basis of ideas of the mechanism of oxidation of ferrocene by iodine, we have suggested that the energy of solvation of the ferricenium ion should be comparatively high. In order to test this suggestion, we report in the present paper a spectrophotometric study of the equilibrium $\text{Fn} + \frac{3}{2} \text{I}_2 = \text{Fn}^+ + \text{I}_3^-$ in alcohol at different temperatures in the range 15-45°. Knowing the heat effect of this reaction, we can calculate the energy of solvation of the ferricenium ion from the corresponding cyclic process.

METHODS AND RESULTS

A sample of iodine and the ferrocene solution were placed in a thermostatically controlled cuvette (d 1.00 cm). The spectrum of the solution was recorded in the region of absorption by the ferricenium ion (580-660 mμ) on a two beam SF2M spectrophotometer. The time of reaching equilibrium in the experiments did not exceed 30 minutes.



Determination of equilibrium constant for the reaction $\text{Fn} + \frac{3}{2} \text{I}_2 = \text{Fn}^+ + \text{I}_3^-$ in alcohol (0.25% water), 616 mμ; layer 1 cm. 1) 15°, 2) 25°, 3) 35°, 4) 45°.

The initial ferrocene concentration was so set that the iodide occurred in the form of triiodide and the ion of the latter was not especially associated with the ferricenium ion. The experiments were carried out with some excess of iodine and at ferrocene concentrations from $2.5 \cdot 10^{-4}$ to 10^{-3} and iodine from 10^{-3} to $1.2 \cdot 10^{-2}$ mole · liter⁻¹. Under equilibrium conditions the ionic strength of the solution did not exceed 10^{-3} mole · liter⁻¹. Therefore in calculating the equilibrium constant it was possible with a sufficient degree of accuracy to take the activity coefficient for ferrocene and iodine as unity, and the activity coefficient of the ions was calculated by the Debye limiting law.

If the reaction $\text{Fn} + \frac{3}{2} \text{I}_2 = \text{Fn}^+ + \text{I}_3^-$ is not complicated by side reactions and the Lambert-Beer law is obeyed for all the molecules and ions present, then the relation between the optical density of the solution D_∞ at equilibrium and the initial concentrations $[\text{Fn}]_0$ and $[\text{I}_2]_0$ is given by the equation

$$[\text{Fn}]_0 (D_\infty - D_0)^{-1} = \Delta \epsilon^{-1} + K^{-1} \Delta \epsilon^{-2} \gamma^2 (D_\infty - D_0) [\text{I}_2]_0^{-3/2},$$

* Fn means $(\text{C}_5\text{H}_5)_2\text{Fe}$.

where: $D_0 = \epsilon_{Fn} [Fn]_0 + \epsilon_{I_2} [I_2]_0$; $\Delta\epsilon = \epsilon_{Fn} + \epsilon_{I_2} - \epsilon_{Fn} \cdot \frac{3}{2} \epsilon_{I_2}$. K is the equilibrium constant, γ the activity coefficient for the singly charged ion, ϵ the absorption coefficient for the molecules or ions, $[I_2]$ the iodine concentration at equilibrium, which differs little from $[I_2]_0$ if the iodine is in excess.

This equation shows that between $[Fn]_0(D_\infty - D_0)^{-1}$ and $\gamma^2(D_\infty - D_0)[I_2]^{-\frac{3}{2}}$ there should be a linear relation. In order to determine $\Delta\epsilon$ and K using this equation it is necessary to know the values of γ and $[I_2]$. The latter were found by the method of successive approximations. In this calculation the initial values were $\gamma=1$ and $[I_2] = [I_2]_0$. In later approximations γ and $[I_2]$ were found by the relationship $[Fn^+] = \Delta\epsilon^{-1}(D_\infty - D_0)$. The figure shows the relation after a series of approximations when the given and obtained values of $\Delta\epsilon$ agree.

TABLE 1

Values of K and $\Delta\epsilon$ for Different Temperatures at λ 616 m μ ; solvent, ethyl alcohol (0.25% water)

Temperature	$\Delta\epsilon$ (cm ⁻¹ · mole ⁻¹ · liter)	K , mole ^{-1/2} · liter ^{1/2}	Number of experiments
15.0°	546	3.75	7
25.0	531	3.15	22
35.0	533	2.32	5
45.0	547	1.53	4

TABLE 2

Thermodynamic Data for Reaction $Fn + \frac{3}{2} I_2 = Fn^+ + I_3^-$ in Alcohol at 25°

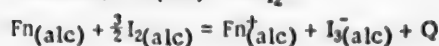
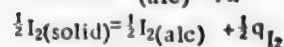
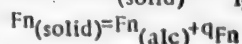
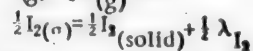
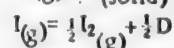
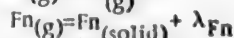
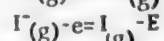
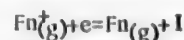
Percent water in alcohol	ΔH° (kcal · mole ⁻¹)	ΔS° (e. u.)	ΔF° (kcal · mole ⁻¹)
0.25	-5.5	-16	-0.675
3.5	-5.5	-14	-1.37

In Table 1 we give the values for $\Delta\epsilon$ and K for different temperatures found by ΔH° , ΔS° , ΔF° for the reaction (Table 2).

From the values obtained for $\Delta\epsilon$ for different wavelengths we determined the absorption coefficients for the ferricenium ion (Table 3).

DISCUSSION OF RESULTS

For finding the solvation energy of the ferricenium ion we consider the cyclic process:



$$I_3(\text{alc}) = I_2(\text{alc}) + I(\text{alc}) + Q_0$$

$$\text{Fn}^+(\text{g}) + I(\text{g}) = \text{Fn}^+(\text{alc}) + I(\text{alc}) + L_{\text{Fn}^+} + L_{I^-}$$

TABLE 3

Absorption Spectra in Alcohol (0.25% water) at 25°

λ (m μ)	$\Delta\epsilon$	I_2	$\epsilon_{\text{Fn}}(\text{cm}^{-1} \times$ $\times \text{mole}^{-1} \cdot \text{l})$	I^-	Fn^+
580	384	47.8	0.8	80	377
600	465	32.3	0.6	53	461
616	531	23.8	0.5	35	532
620	527	22.0	0.5	32	529
640	241	14.8	0.4	18	246
660	51	9.8	0.4	10	56

TABLE 4

Sum of Solvation Energies of Cation M^+ and Anion I^- in Ethyl Alcohol

M^+	Li^+	Na^+	K^+	Rb^+	Cs^+	Fn^+	$(\text{CH}_3)_4\text{N}^+$	$(\text{C}_4\text{H}_9)_4\text{N}^+$
$L_{M^+} + L_{I^-}$ (kcal · mole $^{-1}$)	199	170	162	147**	137**	129	100	90
Ionic radius (Å)	0.60	0.95	1.33	1.48	1.69	—	3.00	3.63

In the calculations we used the following values (in kcal·mole $^{-1}$): $I = 162.5$ [7], $E = 74.6$ [5], $\lambda_{\text{Fn}} = 19.9$ [4], $D = 36.0$ [5], $\lambda_{I_2} = 14.8$ [5], $q_{\text{Fn}} = -5.0$, $q_{I_2} = -1.65$ [6], $Q_0 = -3.6$ [7] for the reaction in water. The value for Q_0 for alcohol could differ from the value for water, evidently, by not more than 2 kcal·mole $^{-1}$. The sum of the solvation energies of ions of ferricenium and iodide $L_{\text{Fn}^+} + L_{I^-}$ is about 129 kcal·mole $^{-1}$. This value in Table 4 is compared with the sum of the solvation energies $L_{M^+} + L_{I^-}$ for other cations M^+ .

From the relation of solvation energy to ionic radius (Table 4) we can determine the effective solvation radius of the ferricenium ion which is equal to about 2 Å. In the electrically neutral ferrocene molecule the distance Fe-C is 2.04 Å; in the ion this distance can be somewhat less. The comparatively small value for the solvation radius and the large solvation energy can be understood if we assume that the positive charge of the ion is chiefly concentrated on the atom of iron.

The oxidation of ferrocene by iodine is of interest as an ionic equilibrium in a nonaqueous medium. Approximate calculations [8] based only on calculation of the electrostatic interaction of the ions with the medium show that with decreased dielectric permeability of the medium the entropy of solvation of the ions should assume a more negative value. This conclusion is confirmed by comparison of the data on dissociation of tetrabutylammonium picrate in chlorobenzene [9] ($\Delta S^0 = 20$ e.u.) and the base of Malachite green in water [10] ($\Delta S^0 = +4$ e.u.). Thus the negative value of ΔS^0 (Table 2) is not unexpected. The relation of solvation entropy of the ion to dielectric permeability of the medium also agrees with our data on equilibrium in alcohol with different water contents. As the data of Table 2 show, lowering the water concentration leads to a decreased ΔS of the reaction.

*Private communication from O. M. Gaissinskaya and V. A. Sokolov.

**Values for methyl alcohol. The sum of solvation energies for other ions in methyl and ethyl alcohols are very close to each other.

The author expresses thanks to Ya. K. Syrkin for aid in this work.

SUMMARY

1. We have determined the equilibrium constants for the reaction of oxidation of ferrocene by iodine in ethyl alcohol at 15, 25, 35, and 45°. We have calculated values for ΔH^0 and ΔS^0 : $\Delta H^0 = -5.5 \text{ kcal} \cdot \text{mole}^{-1}$ and $\Delta S^0 = -16 \text{ e. u.}$

2. We have showed that the solvation energy of the ferricenium ion has a relatively large value.

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*Original Russian pagination. See C. B. translation.

THE REVERSIBLE CROTONIZATION REACTION OF ACETALDEHYDE OVER THE S. V. LEBEDEV CATALYST

S. V. Ivanov and N. M. Maksimova

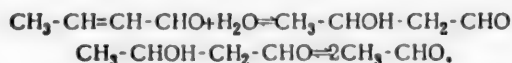
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The process of formation of crotonaldehyde by condensation of acetaldehyde with splitting out of water can be reversed in one step over a solid catalyst in the gas phase. Approximate thermodynamic calculations of the reaction of crotonization of acetaldehyde carried out with account of the dilution of the starting aldehyde by water showed that increase in temperature and decrease in dilution of acetaldehyde by water should aid in the formation of crotonaldehyde [1]. However, even at 200-400° and the absence of dilution according to data of the approximate thermodynamic calculations the equilibrium of the reaction is not absolutely shifted to the side of formation of crotonaldehyde: from 1 mole of taken acetaldehyde by this conversion there results 0.74 mole at 500° and 0.85 mole at 700° K.

The reversibility of the crotonization reaction of acetaldehyde probably goes by analogy with the literature report on the conversion of mesityl oxide with water (up to 32%) into diacetone alcohol and acetone over aluminum oxide and silica gel at 300° [2]. We can assume that the first product of catalytic hydration of crotonaldehyde should be acetaldol which would then depolymerize to acetaldehyde.



We have studied the possibility of the reversible reaction of crotonization of acetaldehyde using the S. V. Lebedev catalyst, and also its dehydrogenating and dehydrating components. As a result of these experiments we have established that crotonaldehyde with water (1 : 6, in moles) over the S. V. Lebedev catalyst at 365° forms acetaldehyde with yields up to 6 weight %, calculated on the crotonaldehyde passed. Control experiments in which crotonaldehyde was submitted to conversion in the absence of water did not lead to formation of acetaldehyde.

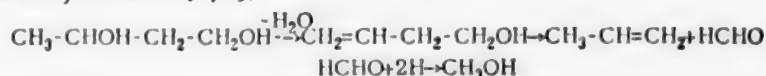
In order to make more exact our understanding of the function of the components of the catalyst in the reversible reaction of crotonization of acetaldehyde, analogous experiments were carried out on the dehydrogenation and dehydration with the components of the S. V. Lebedev catalyst. It was shown that crotonaldehyde forms acetaldehyde with water only over the dehydrating component of the catalyst.

The assumption of the depolymerization of acetaldol formed in the intermediate step in the hydration of crotonaldehyde was confirmed by experiments on direct transformation of acetaldol into acetaldehyde over the S. V. Lebedev catalyst and its dehydrating component at 365°, both in the presence of water and without it.

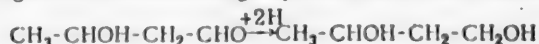


The reversible reaction of crotonization of acetaldehyde which takes place with the dehydrating component of the S. V. Lebedev catalyst can be explained by the assumption of the scheme of formation of methyl alcohol in the catalytic process of preparing divinyl from alcohol. The formation of methyl alcohol in the S. V. Lebedev

process is considered as occurring with decomposition of 1,3-butanediol with formation of formaldehyde which is reduced because of the hydrogen of the alcohol groups. The intermediate product of propylene decomposition of 1,3-butanediol is allyl carbinol [3, 4].



The experiments carried out in the present work confirm the possibility of hydration of crotonaldehyde into acetaldoal which can thus, under the conditions of the S. V. Lebedev process, lead to an increased concentration of acetaldoal, also formed by direct condensation of acetaldehyde. A rather small part of the acetaldoal under the influence of the hydrogen of the alcoholic groups will further be reduced to 1,3-butanediol.



As special experiments showed [3, 4] the addition of acetaldoal and crotonaldehyde to ethyl alcohol under the conditions of the S. V. Lebedev process causes approximately the same increase in yield of methyl alcohol as in the experiments with addition of 1,3-butanediol to ethyl alcohol. Thus, the reaction of hydration of crotonaldehyde can be considered as one of the initial steps in the formation of methyl alcohol in the S. V. Lebedev process.

EXPERIMENTAL

Acetaldoal was prepared by condensation of acetaldehyde in the presence of 3% aqueous alkali [5], b. p. 74-76° (13-14 mm). Crotonaldehyde was obtained by dehydrations of acetaldoal with orthophosphoric acid [6]. B. p. 101-102°, d_4^{20} 0.8553, n_D^{20} 1.4354. According to the literature, b. p. 101.3-102°, n_D^{20} 1.4356 [7].

In the resulting product the content of crotonaldehyde, determined by analysis for unsaturation by the bromide-bromate method was 98.4%; by analysis for the aldehyde group by the hydroxylamine method it was 99.4%.

The experiments were carried out in a catalytic apparatus of the continuous flow type. A quartz tube (length 1 meter, diameter 35 mm) was placed in a furnace at a slope to the plane of the table. In the tube at a temperature plateau ($\pm 2^\circ$) was placed 130 ml of catalyst. Crotonaldehyde and water were supplied from two burets. Acetaldoal was mixed with water at definite ratios and the water solution was supplied from one buret. The temperature was measured with a chromel-copel thermocouple connected to a recording potentiometer EPP-09. The products of the contact reaction were passed through a condenser and a Lunge flask filled with a solution of hydroxylamine hydrochloride to collect the uncondensed acetaldehyde, and were collected in a gasometer over a saturated solution of common salt.

We used the S. V. Lebedev catalyst and its dehydrogenating and dehydrating components [8]. Activation of the catalyst was carried out for six hours at 500-550° with passage of air. Regeneration of the catalyst was carried out at 490-500° in a stream of air to full burning off of carbon from the surface of contact. Since in the experiments with acetaldoal the catalyst was very heavily carbonized, the time of regeneration was up to six hours. The conditions and results of the experiments are given in the table.

In all the experiments the volume of gaseous products was small, and gas analysis was not carried out. Calculation of acetaldehyde in the reaction product was carried out by the hydroxylamine method with summation of the content of acetaldehyde determined in the liquid contact products and in the uncondensed gaseous products by analysis of the contents of the Lunge flask. The latter removed about 10% of the acetaldehyde formed.

The receiver with the liquid products was disconnected from the catalytic apparatus and the substances boiling up to 24° were carefully distilled from it. The distillate taken as acetaldehyde was weighed and characterized by derivatives. In experiments 1-3 this was with dimedon, in experiment 6 with 2,4-dinitrophenylhydrazine. The derivative with dimedon had m. p. 138°, anhydro form 173°; the dinitrophenylhydrazone had m. p. 166°. According to the literature [9] the dimedon derivative of acetaldehyde has m. p. 140°, the anhydro form 174°, the 2,4-dinitrophenylhydrazone, 168°.

For the 2,4-dinitrophenylhydrazone of acetaldehyde we found %: N 24.87; $\text{C}_8\text{H}_8\text{O}_4\text{N}_4$, calculated %: N 24.99.

We express thanks to Yu. A. Gorin for valuable advice in carrying out our work.

Expt. No.	Catalyst	Experimental temperature	Dilution with water (moles)	Passed (in g)		Acetaldehyde obtained (in g)	Yield of acetaldehyde on substance passed (in weight %)
				Start-ing sub-stance	Water		
1	S. V. Lebedev	265°	1 : 6	50.0	77.0	0.92	1.8
2	S. V. Lebedev	365	1 : 6	35.0	54.0	2.11	6.0
3	S. V. Lebedev	365	1 : 12	25.7	80.0	1.17	4.6
4	S. V. Lebedev	365	—	33.0	—	—	—
5	Dehydrogenating component	365	1 : 6	36.0	54.5	—	—
6	Dehydrating component	365	1 : 6	20.5	31.6	0.42	2.0
7	S. V. Lebedev	365	1 : 6	44.0	52.8	1.60	3.6
8	S. V. Lebedev	365	—	39.7	—	4.46	11.2
9	Dehydrating component	365	—	40.9	—	4.71	11.5

Note: In experiments 1-6 the starting substance was crotonaldehyde; in experiments 7-9, acetal-dol. The rate of supplying the starting substance in all experiments was 0.23 ml/hour/ml of catalyst.

SUMMARY

1. We have shown the possibility of a reversible reaction of crotonization of acetaldehyde over the S. V. Lebedev catalyst under the influence of its dehydrating component.

2. This process occurs in intermediate stages through hydration of crotonaldehyde into acetal-dol and depolymerization of the latter.

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STUDIES IN THE FIELD OF COMPOUNDS WHICH CONTAIN
A THREE MEMBERED OXIDE RING
XXV. THE REACTION OF METHYL α -METHYLGLYCIDATE
WITH AROMATIC AMINES

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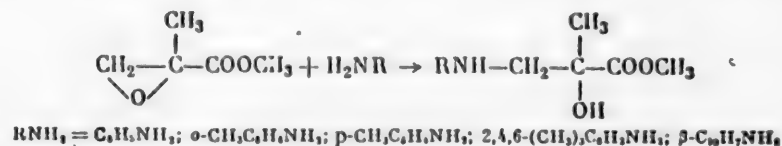
In a series of previous studies [1] we have made a detailed investigation of the reaction of aromatic amines with esters of β -mono and β -disubstituted glycidic acids and have explained the regularities of this reaction. This present work has thrown light on the still untouched question of the study of the rules for opening oxide rings in esters of α -substituted glycidic acids. As the object of study we have chosen the simplest example of this group of compounds, methyl α -methylglycidate. It must be said that suitable methods for the synthesis of this compound do not exist. The Darzens reaction is not very useful here, since separation of the products after running the reaction is very difficult. We obtained the starting glycidic ester by two methods: through the hydroxy-bromo acid and by oxidation of methyl methacrylate with benzoyl hydroperoxide. In the first method the reaction was carried out by reaction of methyl methacrylate with N-bromoacetamide in acid medium, as a result of which we obtained in satisfactory yield methyl α -bromo- β -hydroxy- α -methylpropionate, which then by the action of dry sodium methylate was converted to the glycidic ester.

Oxidation of methyl methacrylate by benzoyl hydroperoxide was carried out by the usual method, as often described for use with various unsaturated compounds. It is necessary to note, however, that the yield of glycidic ester in this case is low.

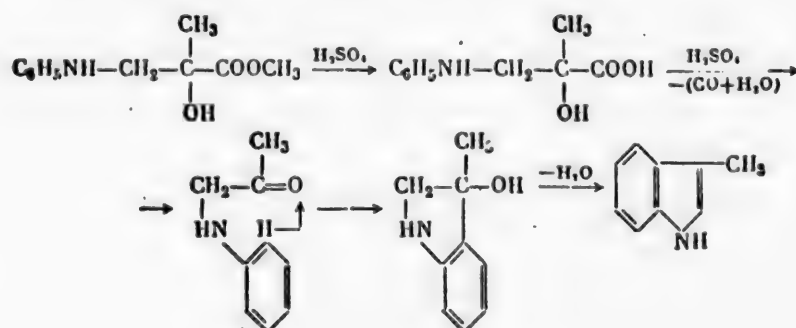
We carried out the reaction of methyl α -methylglycidate with five aromatic amines: aniline, o- and p-toluidines, mesitylamine, and β -naphthylamine. The reaction was run by heating the components in toluene solution, boiling the mixture for several hours. Only with mesitylamine did we carry out the reaction in a sealed tube at 180°. The reaction with the glycidic ester goes more easily than with esters of disubstituted glycidic acids which is evidently because of the lower spacial hindrance occurring during the reaction.

All of the compounds which were obtained were split by heating with concentrated sulfuric acid at a temperature of 80-120° with evolution of carbon monoxide which was identified by qualitative reaction with palladium chloride [2], and also, for the reaction products of the glycidic ester with aniline, o-toluidine and mesitylamine we carried out a quantitative determination of the carbon monoxide evolved in the reaction.

On this basis, that under the influence of sulfuric acid the reaction products split with evolution of carbon monoxide, we can conclude that aromatic amines open the oxide ring of methyl α -methylglycidate on the side of the β -carbon atom, as a result of which there is formed the methyl ester of α -methyl- α -hydroxy- β -arylamino-propionic acid.



Quantitative determination of carbon monoxide showed that the hydroxyarylamino acid obtained in the reaction is not a mixture of two possible isomers, but is one form. Final evidence for the correctness of the above formula can be obtained by isolating the second portion of the molecule, which should be either the corresponding amino ketone or the product of its further transformation, a compound with an indole structure.



In our earlier work, devoted to a study of β -disubstituted β -arylamino- α -hydroxy acids, in the analogous reaction the intermediate carbonyl form, which is the corresponding amino aldehyde, was not separated, since the reaction went further to the formation of compounds with an indole structure. In the decomposition of the methyl ester of β -anilino- α -hydroxy- α -methylpropionic acid we should obtain β -methylindole. This compound, as is known, has a strong fecal odor. However, the crystalline compound which we isolated did not have an unpleasant odor and melted at 75° , while β -methylindole melts at 95° . A mixed sample with known synthetic β -methylindole showed a strong depression of the melting point. We also observed that β -methylindole in strong sulfuric acid with heat gives a dark violet color, while in the decomposition of methyl β -anilino- α -hydroxy- α -methylpropionate with concentrated sulfuric acid such a color does not occur. Thus it was shown that as a result of the reaction there was obtained not β -methylindole, but an amino ketone, anilinoacetone, which was confirmed by analysis for nitrogen; and also with 2,4-dinitrophenylhydrazine we obtained the hydrazone.

For final proof that we had obtained anilinoacetone we synthesized its known 2,4-dinitrophenylhydrazone by the action of the 2,4-dinitrophenylhydrazone of chloroacetone and aniline. The thus prepared 2,4-dinitrophenylhydrazone of anilinoacetone had the same melting point and a mixed sample melted without depression.

By an analogous process and in yield of 55% we obtained *p*-toluidineacetone. Thus, α -arylamino ketones are not condensed by the action of concentrated sulfuric acid into compounds with an indole structure.

EXPERIMENTAL

Methyl α -bromo- α -methyl- β -hydroxypropionate. To 1400 ml of water was added 160 g of *N*-bromoacetamide and 30 ml of concentrated sulfuric acid. The solution was cooled with a mixture of ice and salt and to it was added 76 g of methyl α -methylacrylate and the mixture was stirred for a half hour. The methyl ester was separated in the lower layer in the form of an oily liquid. The water layer was extracted with ether, the ether extract was combined with the main substance and all of it was dried with magnesium sulfate. Distillation gave 116 g of ester as a colorless liquid with b. p. $84-85^\circ$ (3 mm).

Methyl α -methylglycidate. a) In a 500 ml three necked flask was placed a solution of 110 g of methyl α -bromo- α -methyl- β -hydroxypropionate in 300 ml of absolute ether, and at 0° with stirring was added sodium methylate obtained from 14 g of metallic sodium and 23 ml of methyl alcohol. After addition of all the sodium methylate, stirring was continued for six hours at $0-5^\circ$, and then the mixture was heated for four hours under reflux. After cooling, the mixture was treated with ice water, on which the solution separated into two layers. The upper layer, the glycidic ester, was separated and the water layer was extracted with ether. The ether extract was combined with the main substance and dried over sodium sulfate. After distillation we obtained 30 g (47%) of the ester.

b) To 308 ml of a chloroform solution of benzoyl hydroperoxide (containing 26.2 g of $\text{C}_6\text{H}_5\text{COOH}$) was added 19.6 g of methyl α -methylacrylate. The reaction mixture stood in the dark and in a cold place. The course of the reaction was followed by titration with sodium thiosulfate. After about one week almost all the

benzoyl peroxide had reacted. The reaction mixture was washed with a cold solution of NaOH, then twice with water, and was dried over sodium sulfate. After distillation we obtained 7 g (31%) of ester.

Methyl β -anilino- α -methyl- α -hydroxypropionate. Five g of methyl α -methylglycidate and 10.5 g of aniline were dissolved in 20 ml of toluene, several drops of anhydrous alcohol were added, and the reaction mixture was heated under reflux at 120° for four hours. After distillation of the toluene and unreacted aniline, there distilled at 120° (3 mm) the methyl ester in the form of a yellow, oily liquid which quickly crystallized as needles. After recrystallization from ligroin, we obtained 4 g (43.4%) of colorless needles with m. p. 50°.

Found %: N 6.3. $C_{11}H_{15}O_3N$. Calculated %: N 6.6.

Anilinoacetone. To 4 g of methyl β -anilino- α -methyl- α -hydroxypropionate was added 20 ml of concentrated sulfuric acid and the mixture was heated with stirring over a bare flame. At 60-80° bubbles of carbon monoxide began to evolve. Heating was continued at 120° to full stoppage of evolution of CO. Then it was cooled, a small amount of ice water was added, and the mixture was neutralized with barium carbonate to a weakly alkaline reaction. The barium sulfate was filtered off hot and the filtrate was cooled to formation of flat white crystals of anilinoacetone. We obtained 2 g (55%). After recrystallization from ligroin they melted at 75°.

Found %: N 9.18. $C_9H_{11}ON$. Calculated %: N 9.4.

With 2,4-dinitrophenylhydrazine we obtained the hydrazone in the form of fine orange-red crystals which after recrystallization from benzene melted at 180°.

Found %: N 21.28. $C_{15}H_{15}O_4N_5$. Calculated %: N 20.78.

To 0.2 g of the 2,4-dinitrophenylhydrazone of chloroacetone (m. p. 123.5°) was added 0.8 g of aniline and the mixture was heated on the water bath for 10 minutes. After cooling, crystals separated which were washed free of excess aniline and recrystallized from toluene; m. p. 189°. A mixed sample with the hydrazone obtained above melted at 188°.

Methyl ester of β -(p-toluidino)- α -methyl- α -hydroxypropionic acid. Five g of methyl α -methylglycidate, 14 g of p-toluidine, several drops of anhydrous alcohol, and 20 ml of toluene were heated with a reflux condenser at 120° for four hours. After distillation of the toluene and excess toluidine, the methyl ester of the hydroxy-toluidino acid distilled in the form of a yellow, oily liquid with b. p. 149-150° (2 mm), which quickly crystallized. After recrystallization from ligroin, m. p. 67°; yield 8 g (84%).

Found %: N 6.18. $C_{12}H_{17}O_3N$. Calculated %: N 6.2.

p-Toluidinoacetone. Two g of methyl p-toluidino- α -methyl- α -hydroxypropionate mixed with 10 ml of concentrated sulfuric acid was heated at 100° to full stoppage of evolution of bubbles of carbon monoxide. After cooling, the brown solution was poured into a small amount of ice water and neutralized with barium carbonate. The $BaSO_4$ was filtered hot and the filtrate was cooled to appearance of crystals of toluidinoacetone. After recrystallization from ligroin the compound had m. p. 77°. Yield 0.8 g (53%).

Found %: N 8.02. $C_{10}H_{13}ON$. Calculated %: N 8.58.

With 2,4-dinitrophenylhydrazine we obtained the hydrazone as yellow needles which after recrystallization from benzene were obtained as fine red crystals with m. p. 170-171°.

Methyl ester of β -(o-toluidino)- α -methyl- α -hydroxypropionic acid. Five g of methyl α -methylglycidate, 14 g of o-toluidine, several drops of anhydrous alcohol, and 20 ml of toluene were heated with a reflux condenser at 120° for six hours. After the end of the reaction the dark brown, viscous reaction mixture was vacuum distilled. At 126° (2 mm) a substance distilled as a yellow, oily liquid. Yield 2.5 g (26%).

Found %: N 6.45. $C_{12}H_{17}ON$. Calculated %: N 6.2.

Methyl ester of β -(1, 3, 5-trimethylanilino)- α -methyl- α -hydroxypropionic acid. Three g of methyl α -methylglycidate, 4 g of 1, 3, 5-trimethylaniline, and a small amount of anhydrous alcohol were heated in a sealed tube at 180° for six hours. After vacuum distillation of the reaction mixture, the ester distilled at 152-153° (4 mm). After standing for 10 days the substance crystallized as white needles which after recrystallization from ligroin melted at 67-68°. We obtained 2 g (31%).

Found %: N 5.73. $C_{14}H_{21}O_3N$. Calculated %: N 5.5.

Methyl ester of β -(β -naphthylamino)- α -methyl- α -hydroxypropionic acid. Five g of methyl α -methylglycidate, 5 g of β -naphthylamine, 20 ml of toluene, and a small amount of anhydrous alcohol were heated with a reflux condenser at 120° for six hours. After vacuum distillation we obtained 2 g (14.5%) of a substance in the form of a yellow, oily liquid with b. p. 160° at 2 mm.

Found %: N 5.6. $C_{15}H_{17}O_3N$. Calculated %: N 5.4.

SUMMARY

1. We have studied the reaction of methyl α -methylglycidate with aromatic amines. We have showed that opening of the oxide ring of the glycidic acid occurs on the side of the β -carbon atom. As a result of the reaction there is formed the α -hydroxy- β -arylamino acid.

2. We have studied the reaction of the methyl esters of β -anilino- and β -(*p*-toluidino)- α -hydroxy- α -methylpropionic acids with concentrated sulfuric acid when heated. We have showed that in this case there are formed the arylamino ketones: anilinoacetone and *p*-toluidinoacetone respectively.

3. We have showed that the arylaminoacetones under the influence of sulfuric acid are not condensed into compounds with an indole structure.

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*Original Russian pagination. See C. B. translation.

REACTION OF DIACETYLENE WITH AMINO ALCOHOLS AND AMINES

II. SYNTHESIS OF 1,4-N-ALKYLDIAMINO-1,3-BUTADIENES AND 1-N,N-DIALKYL-AMINO-1-BUTEN-3-YNES

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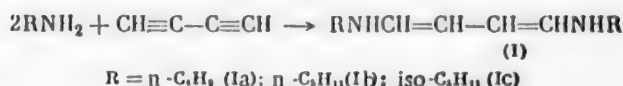
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10,

pp. 3179-3183, October, 1960

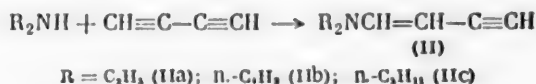
Original article submitted August 4, 1959

In studying the reaction of diacetylene with amino alcohols we have showed [1] that the latter react with diacetylene both by the hydroxyl and amino groups. In the example of β -(diethylamino)-ethanol we have studied the reaction of diacetylene with an amino alcohol which does not contain free hydrogen atoms on the amino group [1, 2]. It was also interesting to study the reaction of diacetylene with amines themselves, since in the literature there is only one patent [3] in which the author reports obtaining 1-N,N-diethyl-3-butenynyl-amine from diacetylene and diethylamine at 45° in the presence of copper or silver salts.

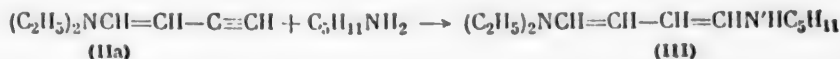
In the present work we give data on the investigation of the reaction of diacetylene with amines, results which were briefly published earlier [4]. It was shown that the reaction of diacetylene with amines of the aliphatic series, like the reaction with β -(dialkylamino)-ethanols, begins at room temperature and proceeds exothermally without a catalyst. Under analogous conditions methylaniline does not react with diacetylene. The nature of the starting amine has an important effect on the direction of the reaction. Thus, a primary amine reacts with diacetylene with formation of 1,4-N-alkyldiamino-1,3-butadiene (I) (yield 80%)



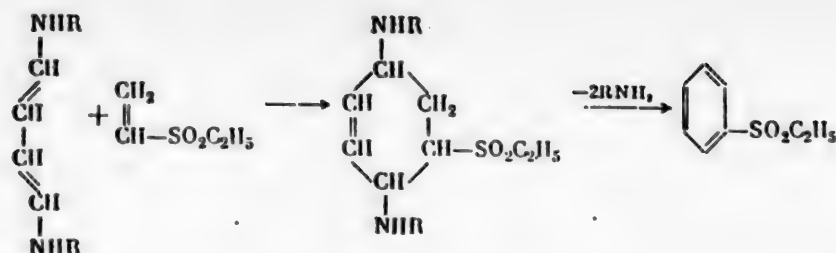
A secondary amine reacts with diacetylene under analogous conditions with formation of 1-N,N-dialkyl-amino-1-buten-3-yne (II) with a yield of 60%.



The addition of amines to ethynylvinylamine (II), evidently because of spacial difficulties, requires more severe reaction conditions. For example, n-amyamine adds to ethynylvinylamine (IIa) on boiling in a vacuum and forms 1,4-N,N-diethyl-1'-amyldiamino-1,3-butadiene (III) (yield 60%).

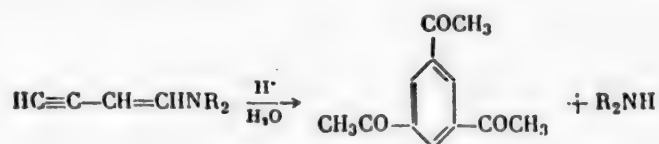


The diene structure of the resulting substances (I) and (III) was shown by spectral analysis and the diene synthesis with ethylvinyl sulfone. From the reaction product of the diene synthesis we isolated ethylphenyl sulfone and alkylamines, the preparation of which can be explained by splitting out during distillation of two molecules of alkylamine from the adduct which first formed.



Such aromatization of the adduct with heat has also been found by other investigators [5] and is evidence of the 1,4-distribution of the substituents in the diene. The symmetrical structure of the butadiene (I) is also confirmed by spectral analysis, since the bands and lines of the double bond were not split. In the case of butadiene (III) there was observed a very intense band, split into two, which could be explained by the presence of different substituents in the substance.

The structure of the products of reaction of diacetylene with secondary amines was shown by hydrolysis, positive reaction for mobile acetylenic hydrogen, and spectral analysis. As a result of hydrolysis with a 2% sulfuric acid solution we obtained triacetylbenzene.



The synthesized compounds (I), (II), and (III) are colorless or yellow, unstable liquids, which, however, can be kept for a long time in sealed ampules at $-50-70^\circ$. Dienes (I) and (III) easily absorb carbon dioxide from the air and form stable solid carbonates which is also characteristic of the starting amines. Spectral analysis of these, confirming the presence of the group $\begin{array}{c} \text{O} \\ // \\ \text{C} \\ \backslash \\ \text{O}^- \end{array}$, showed that the diene structure was here preserved.

The spectroscopic study was carried out by B. V. Lopatin, to whom the authors express thanks.

EXPERIMENTAL

Synthesis of 1,4-N-alkyldiamino-1,3-butadienes (I). In a three necked flask fitted with a stirrer, condenser, thermometer, and bubbling tube was placed 30 g (0.41 mole) of n-butylamine (b. p. $78-79^\circ$, n_D^{20} 1.4041). At $15-20^\circ$ with stirring we passed in diacetylene diluted with nitrogen for two hours. Unreacted diacetylene was passed through the condenser and an absorption flask with 10% sodium hydroxide and was condensed in a trap cooled with a mixture of acetone and solid carbon dioxide. The reaction was exothermic ($40-50^\circ$). About 6 g of diacetylene was absorbed. The reaction mixture was stirred for four hours, kept for twelve hours, and distilled in a vacuum. We separated 12.7 g of unreacted n-butylamine and 19 g of 1,4-N-butyldiamino-1,3-butadiene (Ia). In the residue was 3.6 g of tarry liquid. In an analogous way we prepared butadienes (Ib) and (Ic). In the case of butadiene (Ic) we found strong tarring so that its yield fell to 30%. This can evidently be explained by the effect of the iso-radical. The physicochemical constants and analyses of these compounds are given in the table.

Synthesis of 1-N, N-dialkylamino-1-buten-3-yne (II) was carried out under conditions analogous to those described above. The diacetylene was passed through 30 g (0.4 g mole) of diethylamine (b. p. 55° , n_D^{20} 1.3870). Reaction temperature $30-35^\circ$. Six g of diacetylene was absorbed. When the reaction mixture was distilled we isolated 22.5 g of diethylamine, 8.1 g of 1-N, N-diethylamino-1-buten-3-yne (IIa), and 0.8 g of a fraction (b. p. $98-103^\circ$ at 35 mm) which was studied. The residue contained 3.8 g of a tarry liquid. In an analogous way we obtained the dialkylethynylvinylamines (IIb) and (IIc) (see table).

Characteristics of 1,4-N-Alkylidiamino-1,3-butadienes and 1-N, N-Dialkylamino-1-buten-3-ynes and Their Derivatives

Substance No.	Formula	Yield(%) calc. on reacting start. prod.	B. p. (pressure in mm)	n _D ²⁰	d ₄ ²⁰	Found, %			Empirical formula	Calculated, %			Spectroscopic data (cm ⁻¹)
						C	H	N		C	H	N	
(Ia)	C ₆ H ₁₁ NHCH=CH-CH=CHNHCH ₂ H ₅	80	117°(8)	1.5032	0.8540	73.20	12.21	14.59	C ₁₁ H ₁₉ N ₂	73.40	12.32	14.26	1582*
(Ib)	n-C ₄ H ₉ NHCH=CH-CH=CHNHCH ₂ H ₁₁ -n	80	132 (6)	1.5003	0.8545	75.19	12.38	12.57	C ₁₁ H ₁₉ N ₂	74.96	12.58	12.40	1581*
(Ic)	iso-C ₄ H ₉ NHCH=CH-CH=CHNHCH ₂ H ₁₁ -iso	30	127 (7)	1.4960	—	75.06	12.38	12.54	C ₁₁ H ₁₉ N ₂	74.96	12.58	12.40	—
(IIf)	(C ₄ H ₉) ₂ NCH=CH-CH=CHNHCH ₂ H ₁₁ -n	80	144 (7)	1.4996	0.8555	74.19	12.32	13.06	C ₁₁ H ₁₉ N ₂	74.22	12.45	13.31	1583, ** 1625
(IIa)	(C ₄ H ₉) ₂ NCH=CH-C≡CH***	60	66—68 (9)	1.5177	0.8570	78.26	10.61	11.37	C ₈ H ₁₃ N	77.99	10.63	11.37	2074, * 1612
(IIb)	(C ₄ H ₉) ₂ NCH=CH-C≡CH	60	115 (8)	1.5024	0.8499	80.38	11.68	7.82	C ₈ H ₁₃ N	80.13	11.80	7.81	—
(IIc)	(n-C ₄ H ₉) ₂ NCH=CH-C≡CH	65	139 (7)	1.4992	0.8474	81.08	12.13	6.95	C ₈ H ₁₃ N	81.00	12.15	6.75	2074, ** 1625
—	Carbonate (Ia)	—	M. p. 89—89°	—	—	60.89	9.95	10.87	C ₁₁ H ₁₉ N ₂ · H ₂ CO ₃	60.43	10.14	10.84	1561, ** 1604, 1328
—	Carbonate (Ib)	—	M. p. 87—88°	—	—	63.36	10.57	10.01	C ₁₁ H ₁₉ N ₂ · H ₂ CO ₃	62.90	10.55	9.78	—

* The Raman spectra were taken with a three prism spectrograph ISP-51.

** The infrared spectra were taken in the region 2500-1500 cm⁻¹ on an infrared spectrometer IKS-11 with an NaCl prism.

*** Literature data [3]: b. p. 42-45° (3 mm).

**** For all the substances given in the table we found a large exaltation of molecular refraction (about 3).

Synthesis of 1,4-N, N-diethyl-N'-amyldiamino-1,3-butadienes (III). In a distillation apparatus we placed 6.5 g (0.052 mole) of (IIa) and 9.6 g (0.11 mole) of n-amylamine (b. p. 104°, n_D^{20} 1.4123). The mixture was heated in a vacuum (50-60 mm) for 18 hours. The bath temperature was 40-50°. Distillation separated from the reaction products 7 g of n-amylamine, 2.4 g of starting diethylethynylvinylamine (IIa), and 5.6 g of 1,4-N, N-diethyl-N'-amyldiamino-1,3-butadiene (III). The residue contained 1 g of tarry liquid (see table).

Reaction of butadienes (I) and (III) with ethylvinyl sulfone. In a two necked flask fitted with a condenser and thermometer was placed 5 g (0.025 mole) of 1,4-n-butyldiamino-1,3-butadiene (Ia) and with stirring it was treated with 3 g (0.025 mole) of ethylvinyl sulfone. The reaction took place with spontaneous heating (40-50°). After standing for a day, the reaction mixture (7 g) was distilled in a vacuum ($3.5 \cdot 10^{-2}$). We isolated 0.7 g of n-butylamine (b. p. 75-80°, n_D^{20} 1.4047), 2.5 g of starting butadiene (Ia), and 0.9 g of ethylphenyl sulfone with b. p. 157-158° at 8 mm (literature data [6]: b. p. 300°, 160° at 12 mm). The residue contained 2.2 g of tar.

The diene synthesis with compound (III) and ethylvinyl sulfone took place under analogous conditions. Distillation separated from the reaction product a mixture of diethylamine, amylamine, and ethylphenyl sulfone.

Hydrolysis of 1-N, N-diethylamino-1-buten-3-yne (IIa). When 4 g (0.032 mole) of the product was heated with 160 ml of 2% sulfuric acid solution (the amount of sulfuric acid was calculated on neutralization of the amino groups with a slight excess) to 60-70° for 30 minutes, we obtained 0.8 g (35%) of triacetylbenzene. M. p. 160-161° (from methanol). A mixed sample showed no melting point depression.

SUMMARY

1. We have studied the reaction of diacetylene with amines. We have showed that the conditions and direction of the reaction are determined by the nature of the starting amine. The reaction occurs exothermally without a catalyst.

2. We have worked out a method for synthesis of 1,4-N-alkyldiamino-1,3-butadienes and 1-N, N-dialkylamino-1-buten-3-yne from diacetylene and amines.

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STUDIES IN THE FIELD OF SYNTHESIS AND REACTIONS OF OXYGEN-CONTAINING SILICOORGANIC COMPOUNDS.

IX. SYNTHESIS OF SILICOORGANIC ACETALS WHICH CONTAIN NAPHTHYL

M. F. Shostakovskii, Kh. I. Kondrat'ev, and A. K. Gorban'

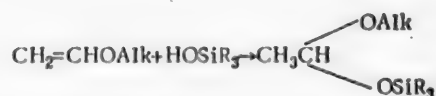
Institute of Organic Chemistry, Academy of Sciences, USSR

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10, pp. 3183-3186,

October, 1960

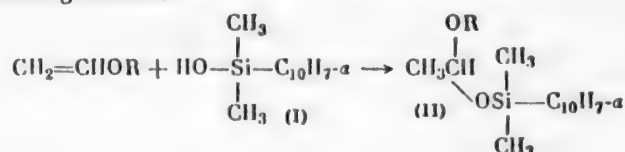
Original article submitted December 14, 1959

We have previously shown that the reaction of vinylalkyl ethers with silanols leads to formation of mixed trialkylsilylalkylacetals [1].



The present investigation is devoted to a study of the reaction of vinyl ethyl, vinyl isopropyl, and vinyl *n*-butyl ethers with α -naphthyldimethylsilanol (I). This was obtained by hydrolysis of α -naphthyldimethylsilyl acetate.

The previous investigation [1] showed that vinylalkyl ethers easily react with silanols by an ionic mechanism in the presence of traces of mineral acids. It was shown, however, that the formation of mixed silico-organic acetals could also occur in the absence of a catalyst. In this case the reaction was characterized by a greater yield since in the presence of acid [1, 2] the side reactions of hydrolysis, dimerization of the silanol, and polymerization of the starting vinyl ether occur to a considerable extent. The structure of the resulting acetals was shown by their hydrolysis with 2% sulfuric acid with formation of α -naphthyldimethylsilanol, acetaldehyde, and the corresponding alcohol.



α -Naphthyldimethylalkylacetals (II) are colorless, easily mobile liquids, soluble in the usual organic solvents and insoluble in water.

EXPERIMENTAL

Dimethyl- α -naphthylsilyl acetate. To 21.2 g of anhydrous sodium acetate in 100 ml of absolute ether at room temperature with energetic stirring was added dropwise during 10 minutes 19 g of dimethyl- α -naphthylchlorosilane* which produced a rise in temperature from 25 to 29°. The reaction mass was stirred for five hours with gentle boiling of the ether. The ether layer was separated and the product after distillation of the

* Obtained from naphthylmagnesium bromide and dimethyldichlorosilane and containing traces of dimethyl- α -naphthylbromosilane.

ether was distilled in vacuum. We obtained 13.4 g (63.7%) of substance.

B. p. 122-125° (1 mm), d_4^{20} 1.0941, n_D^{20} 1.5682, MR_D 73.07; calc. 70.96.

Found %: C 68.81, 68.72; H 6.60, 6.85; Si 11.48, 11.71; acetyl number 22.00, 24.09. $C_{14}H_{16}O_2Si$.
Calculated %: C 68.81; H 6.60, Si 11.48; acetyl number 24.16.

α -Naphthyldimethylsilanol (I). To a mixture of 100 ml of ether, 70 g of ice, 3.5 g of dimethyl- α -naphthylsilanyl acetate and several drops of phenolphthalein solution over a period of 16 minutes with good stirring was added 0.5 N NaOH to weak alkaline reaction. The ether layer was separated, washed with water, and the ether was distilled off. From the residue after removal of the solvent in a vacuum we isolated by recrystallization from heptane and isopentane 1.8 g (62.1%) (I) with m. p. 82-83°. The melting point of a sample mixed with a sample of silanol previously obtained [2] gave no depression.

Found %: C 71.70, 71.67; H 7.03, 7.07; Si 13.90, 14.20. $C_{12}H_{14}OSi$. Calculated %: C 71.24; H 6.98; Si 13.87.

Tetramethyl-di- α -naphthyldisiloxane. When α -naphthyldimethylsilanol was heated at ordinary pressure on a water bath we obtained tetramethyl-di- α -naphthyldisiloxane, a viscous, oily liquid, soluble in acetone, ethanol, diethyl ether; insoluble in water.

B. p. 196° (2 mm), d_4^{20} 1.0878, n_D^{20} 1.5924, MR_D 120.32; calc. 119.50.

Found %: C 74.36, 74.37; H 6.89, 6.80; Si 14.17, 14.03. $C_{24}H_{26}OSi_2$. Calculated %: C 74.56; H 6.78; Si 14.52.

Preparation of α -naphthyldimethylsilylalkylacetals. α -Naphthyldimethylsilylethylacetal. Without a catalyst. In an ampule we placed 2.2 g (0.01 mole) of dimethyl- α -naphthylsilanol with m. p. 82-82.5° and 1.4 g (0.02 mole) of vinyl ethyl ether. The mixture of substances was sealed in and heated on a boiling water bath for about one hour. After the reaction mixture had cooled, the excess vinyl ethyl ether was distilled off and the residue was distilled in a vacuum. We thus obtained 2.2 g (72.8%) of α -naphthyldimethylsilylethylacetal.

B. p. 79-81° at 0.02-0.01 mm, d_4^{20} 1.0321, n_D^{20} 1.5480, MR_D 84.44; calc. 84.78.

Found %: C 69.96, 69.75; H 7.99, 9.92; Si 10.02, 10.28. $C_{16}H_{22}O_2Si$. Calculated %: C 70.03; H 8.08; Si 10.23.

b) In the presence of a catalyst (hydrochloric acid). The corresponding vinylalkyl ether was added with stirring to the silanol. The solution of silanol and vinyl ether occurred with a small amount of heating. Then the reaction mass was cooled to room temperature and a drop of concentrated hydrochloric acid was added to the mixture. The reaction proceeded energetically with a marked evolution of heat. After the solution had cooled it was diluted with ether and the acid was neutralized with potash. After filtration of the product and removal of the ether the residue was distilled in a vacuum. From 7.8 g (0.04 mole) of α -naphthyldimethylsilanol and 3.9 g (0.05 mole) of vinyl ethyl ether we obtained 2.9 g (27.3%) of α -naphthyldimethylsilylethylacetal.

B. p. 125-126° at 2.5 mm, d_4^{20} 1.0403, n_D^{20} 1.5548, MR_D 84.68; calc. 84.78.

α -Naphthyldimethylsilylisopropylacetal. a) Without a catalyst. Two g (0.012 mole) of α -naphthyldimethylsilanol and 12 g (0.14 mole) of vinylisopropyl ether were placed in an ampule which was sealed and heated on a water bath with constant raising of the bath temperature from 55 to 100° in the course of three hours. After cooling, the excess vinylisopropyl ether was distilled off and fractionation of the residue gave 1.3 g (45%) of the substance.

B. p. 85-86° at 0.01 mm, d_4^{20} 1.0284, n_D^{20} 1.5461, MR_D 88.79; calc. 86.50.

Found %: C 70.47, 70.30; H 8.11, 8.12; Si 10.26, 10.10. $C_{17}H_{24}O_2Si$. Calculated %: C 70.79; H 8.39; Si 9.73.

b) In the presence of a catalyst (hydrochloric acid). From 2.2 g (0.012 mole) of α -naphthyldimethylsilanol and 1 g (0.01 mole) of vinylisopropyl ether we obtained α -naphthyldimethylsilylisopropylacetal.

B. p. 134.5° at 3 mm, d_4^{20} 1.0268, n_D^{20} 1.5502, M_R 89.51; calc. 86.50.

α -Naphthylidimethylsilyl-n-butylacetal. a) Without a catalyst. In a flask fitted with a stirrer, thermometer and reflux condenser was placed 10 g (0.05 mole) of α -naphthylidimethylsilanol and to it was added 20 g (0.20 mole) of vinyl-n-butyl ether. Heating of the reaction mixture was carried out with stirring for six hours; the maximum temperature which the reaction mixture reached was 100°. After cooling the reaction mixture, the vinyl-n-butyl ether was distilled off and the residue (15 g) was fractionated. We obtained 13.5 g (90.2%) of α -naphthylidimethyl-n-butylacetal.

B. p. 89-90° at 0.004 mm, d_4^{20} 1.0097, n_D^{20} 1.5350, M_R 93.25; calc. 92.13.

Found %: C 71.41, 71.70; H 8.65, 8.85; Si 9.55, 9.80. $C_{18}H_{26}O_2Si$. Calculated %: C 71.47; H 8.66; Si 9.28.

b) In the presence of a catalyst (hydrochloric acid). From 3.2 g (0.02 mole) of α -naphthylidimethylsilanol and 7.2 g (0.07 mole) of vinyl-n-butyl ether we obtained α -naphthylidimethylsilyl-n-butylacetal with b. p. 112-113° at 1 mm, n_D^{21} 1.5335. At the same time we obtained 2.8 g (50%) of the polymer of vinyl-n-butyl ether.

Hydrolysis of α -naphthylidimethylsilylalkylacetals (II). A sample of the acetal in a small, thin walled ampule was placed in a large ampule with a capacity of 150 ml, with 20 ml of 2% sulfuric acid and 10 ml of 0.4 N solution of sodium bisulfite. The ampule was sealed and the small ampule was broken by shaking. The ampule was shaken at room temperature, then opened and the contents titrated with a 0.1 N solution of iodine in the presence of starch. The results of the hydrolysis are given in the table.

Hydrolysis of α -Naphthylidimethylsilylalkylacetals

Formula and name of acetal	Weight (in g)		a	b	a - b	K	M	Findings, based on acetal, in %
$CH_3CH(OC_6H_4)OSi(CH_3)_2C_{10}H_7-\alpha$ α -Naphthylidimethylsilyl-ethylacetal	0.1892 0.1700	12 11	53.4 53.4	40.4 42.7	13 10.7	0.99425 0.99425	274.396 274.396	93.7 85.86
$CH_3CH(OC_6H_4-isop)OSi(CH_3)_2C_{10}H_7-\alpha$ α -Naphthylidimethylsilyl-isopropylacetal	0.20655	11	53.4	42.5	10.9	0.99425	288.422	75.66
$CH_3CH(OC_6H_4-n)OSi(CH_3)_2C_{10}H_7-\alpha$ α -Naphthylidimethylsilyl-n-butylacetal	0.3276 0.1546	11 9	53.4 53.4	34.6 45.9	18.8 7.5	0.99425 0.99425	302.448 —	86.23 73.04

Calculations were made by the formula: % acetal = $(a-b)K \cdot M / 200 \cdot \text{sample}$, where a is the amount of iodine (ml) used in the control experiment, b the number of ml of iodine used in the experiment with the sample, M the molecular weight of the substance, K a correction for the 0.1 N solution of iodine.

SUMMARY

1. We have showed that the formation of mixed silicoorganic naphthyl-containing acetals prepared from α -naphthylidimethylsilanol and vinyl ethers can occur in the absence of a catalyst (mineral acid).

2. We have synthesized for the first time the ethyl, isopropyl, and n-butylidimethyl- α -naphthylsilylacetals, α -naphthylidimethylsilyl acetate, and tetramethyl-di- α -naphthylidisiloxane.

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STUDIES IN THE FIELD OF THE CHEMISTRY OF FREE RADICALS
OF THE HYDRAZINE SERIES.

III. SYNTHESIS AND PROPERTIES OF N-CARBAZYLPICRYL NITROGEN AND ITS HALOGEN DERIVATIVES

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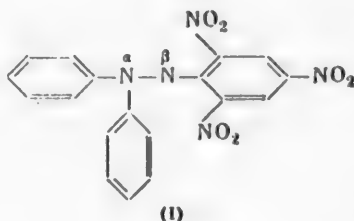
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The electron magnetic resonance spectrum of the hyperfine structure of the stable radical α, α -diphenyl- β -picrylhydrazyl (dpph) (I) shows that in it the unpaired electron on N^β does not react with the π -electrons of the picryl and diphenylamino residues [1]*.

In distinction from the triphenylmethyl radical where the stability depends to a considerable extent on just such a reaction of an unpaired electron with the π -electrons of the phenyl residues, here the stability is determined chiefly by the reaction between the unpaired electron of one atom (N^β) with the unshared (p) electron pair of the other nitrogen atom (N^α).



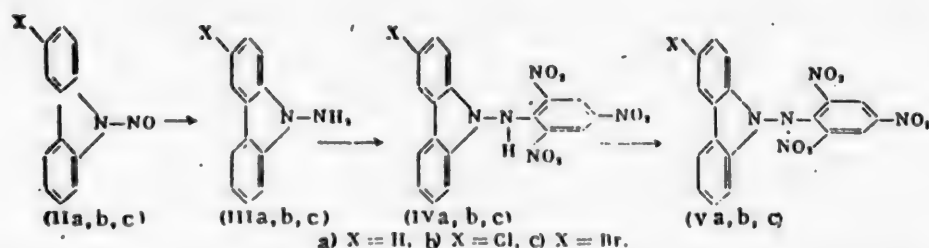
This agrees with the conclusions which were made on the basis of the study of dpph by the method of electron paramagnetic resonance, according to which the cloud of unpaired electrons was evenly distributed between N^α and N^β [3], although each of nitrogen atoms was bound to a different radical (picryl and phenyl). Finally, the reaction between the electrons of N^α and N^β affected the aryls bound to N^α , depending on their electron and spacial structures. Thus, if dpph had the diphenylamine radical replaced by a known coplanar carbazyl radical, this would produce a considerable change in the hyperfine structure of the electron magnetic resonance spectrum. According to the data [4], the electron cloud of unpaired electrons in this radical are distributed also between two nitrogen atoms, but unequally, and are shifted to one of the nitrogen atoms.

This very interesting relatively stable radical has been little studied. In the literature known to us its synthesis is not described, although there are data on its paramagnetic properties.

It therefore seemed important to us for the study of the relation between properties of free hydrazyl radicals and their structure to investigate the properties of the carbazyl radical and also its 3-chloro- and 3-bromoderivatives for comparison of its properties with those of the diphenyl radical [5, 6].

* This is also confirmed by the absence of the "Knight shift". The presence of such a shift indicates the reaction of an unpaired electron with the nucleus of a ring atom [2].

The synthesis of N-carbazylpicrylnitrogen (cpn) and its halogen derivatives was carried out by the following scheme.



To obtain the starting 3-chloro- and 3-bromocarbazoles we first studied the method of converting 3-amino-carbazole into a halogen derivative through the diazo compound [7]. The yield of halogen derivative by this method was 30-35%. 3-Chlorocarbazole was obtained in better yield (70-80%) by chlorination of carbazole with freshly prepared sulfuryl chloride in chloroform [8].

3-Bromocarbazole was obtained with a yield of 80% by the action of succinyl bromide on carbazole in the presence of benzoyl peroxide in carbon tetrachloride [9]. The N-nitrosocompound of the halogen derivatives (IIb, c) were obtained by nitroso formation from the corresponding halocarbazoles with sodium nitrite in glacial acetic acid. The nitrosocompounds were reduced to the N-aminocarbazoles (IIIb, c) with zinc dust in acetic acid at 3-8°. At higher temperatures there was considerable denitrosization and formation of the original 3-halo-carbrazoles.

N-(3-chlorocarbaryl)- and N-(3-bromocarbaryl)-picrylamine (IVb, c) were obtained with almost quantitative yields by the action of the amines with picryl chloride in chloroform solution in the form of crystals with a red or orange color. Oxidation of the amines with lead peroxide in anhydrous chloroform gave radicals (Vc, b) which, like the unsubstituted radical (Va) were crystalline products with an almost black color. They were easily soluble in chloroform and xylene, and formed solutions with an intense blue color.

It is interesting to see that the radicals of the carbaryl series were considerably more active than dpph, dehydrogenating hydroquinone, aromatic amines, and a number of other compounds in solution and themselves being converted to the original amines (IVa, b, c). It seems to us that this effect deserves special study.

Using the method of electron magnetic resonance, we studied in the crystalline samples of the synthesized compounds the exchange reactions of the unpaired electron. The resulting resonance absorption curve for cpn and for comparison that of dpph are given in Fig. 1. The width of the absorption curve between the point of maximum slope ($\Delta H_{m.s.}$) [10] and the ratio of the fourth moment to the second, which characterizes the value of the exchange reaction, are given in Table 1. For comparison, we give the corresponding values for dpph and its halogen derivatives.

TABLE 1

N-(3-X-carbaryl)-picryl nitrogen			α -(p-X-phenyl)- α -phenyl- β -picrylhydrazone		
substituent X	value of $\Delta H_{m.s.}$ (in oersteds)	M_4/M_2	substituent X	value of $\Delta H_{m.s.}$ (in oersteds)	M_4/M_2
H	0.550 ± 0.002	1.63 ± 0.02	H	1.00 ± 0.011	1.43 ± 0.02
Cl	0.725 ± 0.002	1.48 ± 0.02	Cl	1.20 ± 0.15	1.42 ± 0.02
Br	1.150 ± 0.002	—	Br	2.20 ± 0.15	1.40 ± 0.02

Study of cpn was carried out both for a pressure of $5 \cdot 15^{-5}$ mm and at atmospheric pressure in air. The observed difference in width of the line ($\Delta H_{m.s.}$) was small, not more than 4%^{*}; therefore we could obtain the desired comparative data by determination of ΔH at atmospheric pressure in air.

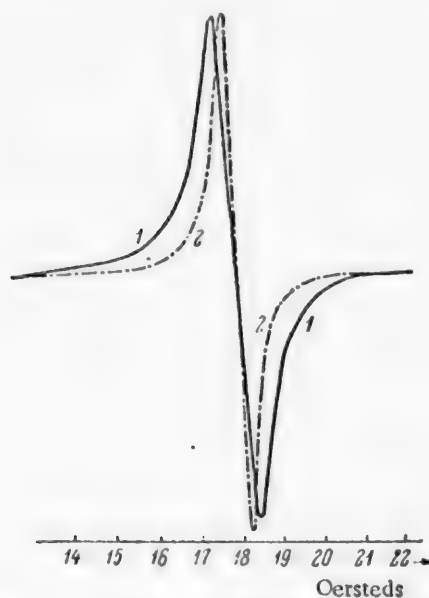


Fig. 1. Curves of resonance absorption: α, α -diphenyl- β -picrylhydrazyl (1) and N-carbazylpicryl nitrogen (2).

derivatives (see Table 1) shows the greater exchange reaction in the crystalline state of the carbazyl radical as compared to the exchange reaction of the phenyl radical. This can have two reasons. First, the constitutive effect of the carbazyl radical in cpn is different from the diphenylamino radical in dpph, since in the carbazole radical the unshared pair of electrons of the nitrogen atom in the ring has a greater possibility of combining with the π -electrons of the ring than the unshared pair of electrons of the N^{β} -atom of nitrogen in diphenylamine. Second, the difference between carbazole and phenyl radicals is also caused by spacial factors which in this case have a primary value if we consider that the measurement of ΔH concerns substances in the crystalline state.

We must assume that the planar structure of the carbazole radical assures a denser packing of the molecule in the crystal and in connection with this the possibility of a greater exchange reaction between the molecules than occurs in the dpph crystals.

Here it should be mentioned that in picrylhydrazine and corresponding radicals the volume of the picryl portion makes impossible the coplanar distribution of the residue bound with the nitrogen atom of the hydrazine. This is clearly evident in Fig. 2, where are shown the models of the molecules of dpph and cpn (in the most planar configurations of the residues).

The ideas expressed here as to the structure of the hydrazyl radical in space naturally require further correction by x-ray structural analysis. Also for a more complete judgment of the role of constitutive factors (effect of one or another group, etc.) on the properties of the radicals, a study of the exchange reactions of the radicals, including those described previously by us [5, 6], should be carried out in solutions where the intermolecular exchange reactions are strongly decreased.

* Analogous to that found for large crystalline forms of dpph [11].

** The effect of g-factor anisotropy of monocrystals on the width of the line of crystalline samples will be discussed in detail by one of us in another place.

A study of the forms of the line of electron magnetic resonance in crystalline samples in a strong field ($H_0=8000$ oersted) showed that the width of the line at half height $\Delta H_{\frac{1}{2}}$ for cpn was 7 oersted while for dpph, $\Delta H_{\frac{1}{2}}=3.7$ oersted. Study of these radicals in a weak field ($H_0=20$ oersted) carried out in our work showed that for cpn $\Delta H_{\frac{1}{2}}=0.95$ oersted, and for dpph, $\Delta H_{\frac{1}{2}}=1.7$ oersted (at a width between the points of maximum slope of 0.55 and 1.0 oersted respectively).

In comparing the width of the lines ΔH of the carbazyl and phenyl radicals in strong and weak fields it was shown that the values of ΔH for cpn in a strong field were larger than for dpph, and on the contrary, the values of ΔH for dpph in a weak field were larger than those for cpn. This can be explained if we assume an effect of the g-factor anisotropy of the monocrystals of these radicals on the width of the line. The latter leads to an increase in width of the line with increasing magnetic field^{**}. In this connection the study of electron paramagnetic resonance of both the phenyl radical and the radical described in our work was carried out under the same conditions—in a weak field ($H=20$ oersted) where the effect of anisotropy of the monocrystals can be neglected.

The lower values of ΔH for cpn and its chloro- and bromo-derivatives as compared with dpph and its corresponding halogen

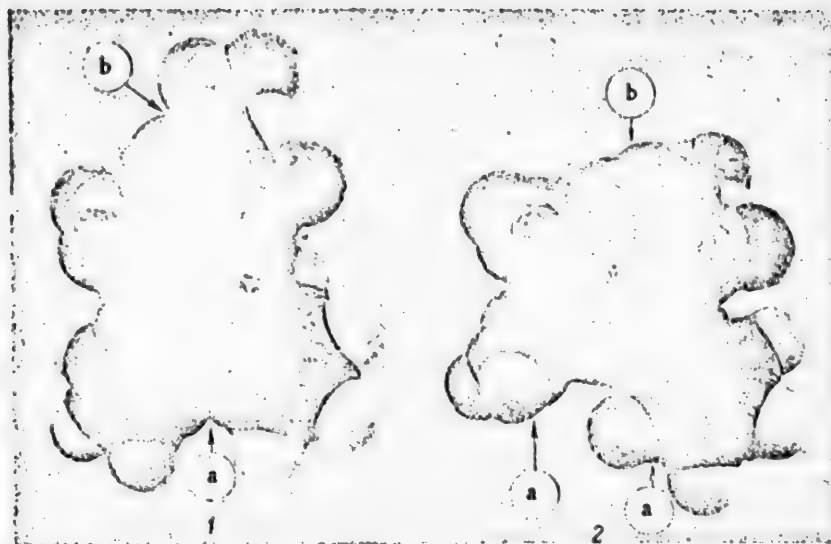


Fig. 2. Models of the molecules: N-carbazylpicryl nitrogen (1) (a is carbazyl, b is the picryl residue), and α,α -diphenyl- β -picrylhydrazyl (2) (a,a are phenyls, b is the picryl residue).

EXPERIMENTAL

3-Chlorocarbazole. Twelve g of freshly distilled sulfonyl chloride and 12 g of carbazole in 200 ml of carbon tetrachloride were boiled on a water bath for one hour. Yield 10 g (70%). M. p. 199-202° (from alcohol), 201-205° [8].

3-Bromocarbazole. A mixture of 16.7 of pure carbazole with m. p. 246°, 17 g of N-bromosuccinyl bromide, 0.18 g of benzoyl peroxide and 270 ml of carbon tetrachloride was boiled on a water bath for one hour. After cooling, a precipitate came down and was filtered off and heated with water to remove succinyl amide. Yield 19 g (78%). M. p. 196-198° (from alcohol), 198-199° [9].

3-X-N-Nitrosocarbazoles (IIb, c). To a solution of 0.02 mole of 3-X-carbazole in glacial acetic acid during one hour was added with stirring 0.03 mole of sodium nitrite; then stirring was continued for two more hours and at 40-45° was added another 0.005 mole of sodium nitrite. The reaction mass was cooled to 8-10° and the precipitate which formed was filtered off. After crystallization from ligroin (b. p. 50-60°) light green crystals were isolated. The resulting nitrosocompounds were easily soluble in hot alcohol, ether, and poorly so in benzene. In concentrated sulfuric acid the nitrosocompounds dissolved with an intense green color. The data of analysis and properties of the nitrosocompounds are given in Table 2.

3-X-Aminocarbazoles (IIIb, c). To a solution of 0.12 mole of 3-X-N-nitrosocarbazoles in ether was added three times the amount by weight of glacial acetic acid. At a temperature not above 8-10° and energetic stirring we gradually added 1.2 mole of zinc dust. The mixture remained standing with stirring for two hours, then the solid was separated and the ether solution, after washing with a saturated soda solution, was dried with calcium chloride. The 3-X-N-aminocarbazole was separated from the ether solution in the form of the hydrochloride by passing in a stream of dry hydrogen chloride. The resulting hydrochloride was transformed into the free base by treatment with a hot alcoholic solution of 25% ammonia. The amine precipitated from the cooled solution. After crystallization from alcohol we obtained colorless crystals, easily soluble in ether, chloroform, dioxane, poorly soluble in cold alcohol. The 3-X-N-aminocarbazoles dissolved in concentrated sulfuric acid with an intense blue color. The halogen derivatives of N-aminocarbazole give good yields of the corresponding azomethine with p-nitrobenzaldehyde (Table 2).

N-(3-X-Carbazyl) picrylamines (IVa, b, c). To a solution of 0.1 mole of N-3-X-carbazylamine in chloroform was added a solution of 0.05 mole of picryl chloride in chloroform. The reaction mass at once became colored an intense red. The resulting mixture was boiled on a water bath for 20-30 minutes, then the chloroform

TABLE 2

Name	Yield, %	Form of crystals (under microscope)	M. p.	Empirical formula	% N	
					found	calculated
3-Chloro-N-nitrosocarbazole (IIb)	70-75	Light yellow needles	130-132°	C ₁₂ H ₇ O ₂ N ₂ Cl	12.37	12.30
3-Bromo-N-nitrosocarbazole (IIc)	69-73	Light yellow needles	133-135	C ₁₂ H ₇ O ₂ N ₂ Br	10.40	10.18
3-Chloro-N-aminocarbazole (IIId)	45-50	Colorless prisms	109-111	C ₁₂ H ₉ N ₃ Cl	13.04	12.96
3-Bromo-N-aminocarbazole (IIId)	43-48	Long colorless prisms	103-105	C ₁₂ H ₉ N ₃ Br	10.98	10.72
N-(4-Nitrobenzalamino)-(3-chlorocarbazole)	90-95	Fine orange needles	210-211	C ₁₈ H ₁₂ O ₃ N ₃ Cl	12.06	12.03
N-(4-Nitrobenzalamino)-(3-bromocarbazole)	90-93	Red needles (clumps)	235-237	C ₁₈ H ₁₂ O ₃ N ₃ Br	10.50	10.69
N-Carbazylpicrylamine (IVa)	73-75	Large red prisms	239-241 *	C ₁₈ H ₁₁ O ₆ N ₅	19.04	17.81
N-(3-Chlorocarbazyl)picrylamine (IVb)	68-70	Orange prisms	235-237 *	C ₁₈ H ₁₀ O ₆ N ₅ Cl	16.51	16.44
N-(3-Bromocarbazyl)picrylamine (IVc)	75-78	Orange prisms	209-211 *	C ₁₈ H ₁₀ O ₆ N ₅ Br	14.98	14.83
N-Carbazylpicryl nitrogen (Va)	65-70	Fine, almost black crystals	215-217 *	C ₁₈ H ₁₀ O ₆ N ₅	17.92	17.81
N-(3-Chlorocarbazyl)picryl nitrogen (Vb)	68-72	Fine, almost black crystals	205-208 *	C ₁₈ H ₉ O ₆ N ₅ Cl	16.51	16.44
N-(3-Bromocarbazyl)picryl nitrogen (Vc)	63-65	Fine, almost black crystals	195-198 *	C ₁₈ H ₉ O ₆ N ₅ Br	14.96	14.86

* With decomposition.

was distilled off to 1/3 the original volume. To the contents of the flask was added twice its amount of hot alcohol, and the resulting solution was boiled for 20-30 minutes. A crystalline precipitate of the picrylamine gradually precipitated. The brick red precipitate which formed was filtered off from the hot solution and crystallized from a mixture of chloroform and alcohol (1 : 3). The picrylamines were easily soluble in chloroform, poorly so in benzene, insoluble in alcohol (Table 2).

N-(3-X-Carbazyl) picryl nitrogen (Va, b, c). To a solution of 0.05 mole of N-(3-X-carbazyl) picrylamine in dry chloroform was added 20 times the amount (by weight) of lead dioxide and 0.5 mole of ignited sodium sulfate. The reaction mass was shaken for 1.5-2 hours. The dark violet solution was separated from the solid, and chloroform was distilled from the mother liquor in a vacuum to formation of a crystalline paste. After filtration, the crystals of the radicals were dried at room temperature in a vacuum. They dissolved well in chloroform and xylene with a blue color, poorly in carbon tetrachloride. On solution in benzene even in 10-15 minutes the radical at room temperature changed markedly into the starting orange red carbazylpicrylamine (in distinction from dpph, which does not dehydrogenate benzene) (see Table 2).

SUMMARY

1. We have synthesized the previously undescribed free radicals of the carbazyl series: N-(3-chlorocarbazyl) picryl nitrogen and N-(3-bromocarbazyl) picryl nitrogen.
2. By the method of electron paramagnetic resonance we have showed that in a weak field ($\Delta H_0 = 20$ oersteds), N-carbazylpicryl nitrogen and also its 3-chloro- and 3-bromo derivatives have in the crystalline form a considerably lower value for the exchange reaction than α, α -diphenyl- β -picrylhydrazyl and its corresponding halogen derivatives.
3. We have suggested ideas on the role of the constitutive and spacial factors which affect the properties of the carbazyl radicals.

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HYDROLYTIC SPLITTING OF SOME SULFONES OF THE HETEROCYCLIC SERIES

VI. SYNTHESIS AND PROPERTIES OF *p*-NITROPHENYLSULFONYL-N-METHYLBENZIMIDAZOLYL-METHANE AND *p*-NITROPHENYLSULFONYLBENZTHIAZOLYLMETHANE

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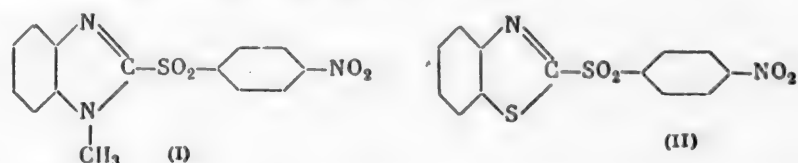
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10,
pp. 3193-3196, October, 1960

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As was shown earlier [1, 2], heterocyclic sulfones which have a sulfoazomethine group $\left(\begin{array}{c} -N \\ \diagup \\ C-SO_2-R \end{array} \right)$ undergo hydrolytic splitting when boiled with dilute alkali or acid according to the scheme

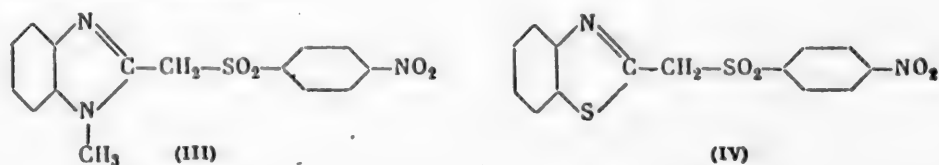


Among the various heterocyclic sulfones *p*-nitrophenyl-N-methylbenzimidazolyl sulfone (I) and *p*-nitrophenylbenzthiazolyl sulfone (II) were obtained [2].

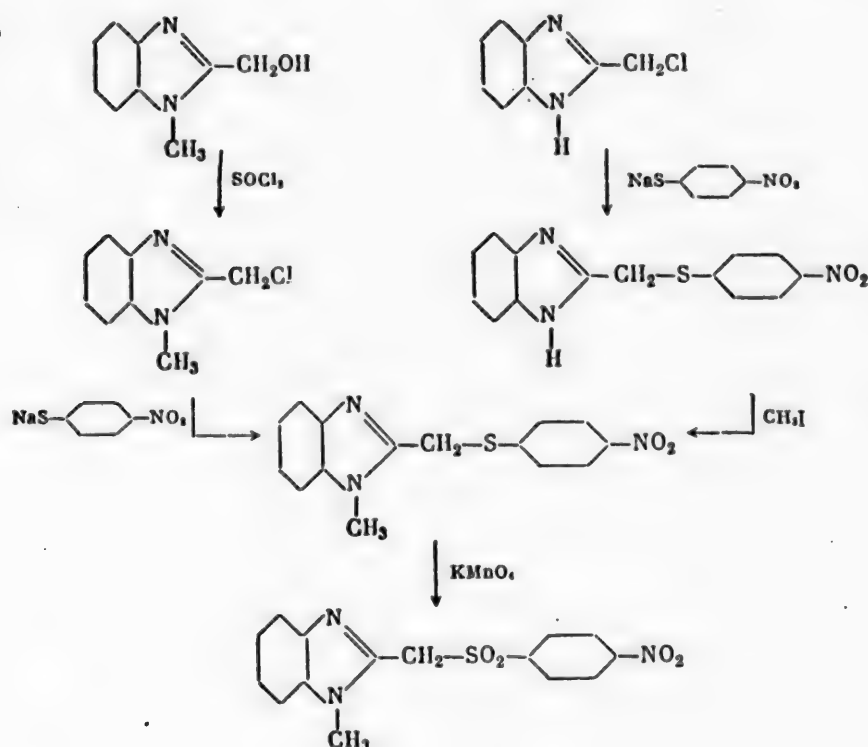


These sulfones are split when heated to 100° with 2 N NaOH in half an hour to the extent of about 50%. The reason for the weak bond C-S in sulfones of this type is the effect on this bond of the two electronegative groups, sulfone (SO₂) and azomethine $\left(\begin{array}{c} -N \\ \diagup \\ C- \end{array} \right)$, which attract the electrons of the bond in two opposite directions approximately the same as occurs in chloral. We can assume that in sulfones which differ from these in that the sulfone group is separated from the azomethine group by a methylene bridge, because of the weakening of the electron acceptor effect of the SO₂ group and the $\begin{array}{c} -N \\ \diagup \\ C- \end{array}$ group, there should be an increase in stability to hydrolysis.

To test this assumption we synthesized *p*-nitrophenylsulfonyl-N-methylbenzimidazolylmethane (III) and *p*-nitrophenylbenzthiazolylmethane (IV).



In the synthesis of these sulfones we started from the chloromethyl derivatives of the benzazoles and sodium *p*-nitrothiophenolate, which easily gave the corresponding sulfides; these were then oxidized to the sulfones. For benzylimidazole sulfone we carried out two variants of the synthesis according to the following scheme:



Sulfones (III and IV) showed great stability to hydrolysis in an acid medium. After two hour heating at 100° in 2 N HCl both sulfones were recovered quantitatively without change.

In comparative hydrolysis in an alkaline medium, the benzimidazole sulfone (III) also remained unchanged and was recovered quantitatively, but the benzothiazole sulfone (IV) heated with 2 N NaOH gradually resinified and was converted to a dark, solid lump, that is, it evidently underwent some sort of condensation.

EXPERIMENTAL

1-Methyl-2-hydroxymethylbenzimidazole. 2-Hydroxymethylbenzimidazole (11 g) (obtained from *o*-phenylenediamine and glycolic acid [3]) was methylated with methyl iodide (8 ml) by boiling in an alcohol solution (20 ml) with 2 N NaOH (25 ml). After cooling, colorless leaflets precipitated from the reaction mass. Yield 60-65%. M. p. $125-130^\circ$ (from water), 105° [4].

1-Methyl-2-chloromethylbenzimidazole. Four g of 1-methyl-2-hydroxymethylbenzimidazole was slowly mixed with 5 ml of thionyl chloride with cooling. At the end of the stormy reaction we obtained a viscous mass which gradually solidified. The hydrochloride was obtained in quantitative yield, m. p. $195-196^\circ$. The base had m. p. 94° (94° [4]).

***p*-Nitrophenylsulfido-N-methylbenzimidazolymethane.** 1) We added gradually 4.5 g of 1-methyl-2-chloromethylbenzimidazole to a warm solution of 4.5 g of sodium *p*-nitrothiophenolate in 70 ml of alcohol. The red brown solution of *p*-nitrophenolate quickly disappeared and the solution became pinkish. Large red needles slowly precipitated. Yield 5.5 g, m. p. $154-155^\circ$ (from alcohol, yellowish needles).

Found %: N 14.26. $\text{C}_{15}\text{H}_{13}\text{O}_2\text{N}_3\text{S}$. Calculated %: N 14.00.

2) We added gradually 6.2 g of 2-chloromethylbenzimidazole, m. p. 165° [4], to a warm solution of 7.1 g

of sodium p-nitrothiophenolate in 100 ml of alcohol. At the end of the addition the solution had decolorized and a light yellow precipitate appeared. Yield 6.7 g. M. p. 214-217°. By dilution of the filtrate with water we obtained another 2.5 g of impure substance (total yield nearly quantitative). Insoluble in dilute NaOH and HCl. Soluble in glacial acetic acid and alcohol.

Found %: N 14.72. $C_{14}H_{11}O_2N_3S$. Calculated %: N 14.73.

The thus obtained p-nitrophenylsulfidobenzimidazolymethane was methylated with methyl iodide in an alcoholic-alkaline medium by a half hour boiling, and was converted in good yield into a sulfide with m. p. 154-155°, identical with that obtained by method 1.

p-Nitrophenylsulfonyl-N-methylbenzylimidazolymethane. Five g of the sulfide, m. p. 154-155°, was dissolved in 100 ml of glacial acetic acid and the solution was cooled with ice. By drops we added an aqueous $KMnO_4$ solution, saturated cold, about 50 ml. The course of the oxidation was followed by the browning of the permanganate. At the end of the reaction the brown mass was decolorized with a solution of sodium bisulfite. For precipitation of the sulfone we added 100-150 ml of water. Long colorless prisms precipitated. Yield 3.5 g. M. p. 223-225° (from alcohol). Poorly soluble in boiling alcohol, better in glacial acetic acid.

Found %: N 12.72. $C_{15}H_{13}O_2N_3S$. Calculated %: N 12.65.

p-Nitrophenylsulfonylbenzthiazolymethane. Chloromethylbenzthiazole was obtained [5] from 2-hydroxy-methylbenzthiazole, which in its turn was obtained from glycolic acid and o-aminothiophenol [6]. Eight g of chloromethylbenzthiazole was dissolved in 20 ml of alcohol and gradually added to a solution of 5 g of sodium p-nitrothiophenolate in 50 ml of hot alcohol. The reaction mass was boiled on a water bath for half an hour, and from dark brown became clear pale yellow. On cooling there precipitated large red-yellow crystals of p-nitrophenylsulfidobenzthiazolymethane. Yield 6 g. M. p. 122-125°. Poorly soluble in alcohol, easily soluble in glacial acetic acid and dioxane. After recrystallization from a mixture of alcohol and dioxane (1 : 1), m. p. 129-130°.

Found %: N 9.20; S 21.24. $C_{14}H_{10}O_2N_2S_2$. Calculated %: N 9.27; S 21.21.

One g of the sulfide with m. p. 129-130° was dissolved with gentle heating in 70 ml of glacial acetic acid (5 ml of water was added to prevent crystallization of the solution on cooling). The solution was cooled to +5° and gradually treated by drops with a cold saturated solution of potassium permanganate (about 25 ml). At the end of the reaction (appearance of permanganate color) the brown reaction mixture was decolorized with a solution of sodium bisulfite and the sulfone was precipitated with water. Yield 0.7 g. M. p. 209-210°. Soluble in glacial acetic acid, poorly in alcohol, well in dioxane. After recrystallization from dilute aqueous dioxane (1 : 1), m. p. 210-212°.

Found %: N 8.33; S 19.18, 18.91. $C_{14}H_{10}O_4N_2S_2$. Calculated %: N 8.38; S 19.18.

Hydrolytic splitting. A sample of 0.50 g of the sulfones was heated in a water-salt bath at 100° (in the bath) with 25 ml of 2 N HCl for two hours. The sulfone of benzimidazole dissolved (evidently with formation of an unstable hydrochloride) but on cooling it precipitated unchanged. Both sulfones were recovered in unchanged form with losses not exceeding 0.01 g. On heating in 2 N NaOH after one hour the benzothiazole sulfone was converted to a lump of dark tar; the benzimidazole sulfone remained unchanged.

SUMMARY

We have synthesized p-nitrophenyl-N-methylbenzimidazolymethane and p-nitrophenylbenzthiazolymethane sulfones. We have shown that these heterocyclic sulfones which contain the group $\text{--}\overset{\text{N}}{\text{C}}\text{--CH}_2\text{--SO}_2\text{--R}$ are stable to hydrolytic splitting in distinction from similar sulfones which contain the grouping $\text{--}\overset{\text{N}}{\text{C}}\text{--SO}_2\text{--R}$ which are easily hydrolyzed at the C-S bond.

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SUBSTITUTED DIACETYL DERIVATIVES OF 1,4- AND 1,5-NAPHTHYLENE-DIAMINES WHICH CONTAIN QUATERNARY AMMONIUM GROUPS IN THE ACETYL PORTION

N. V. Khromov-Borisov and V. A. Ivanova

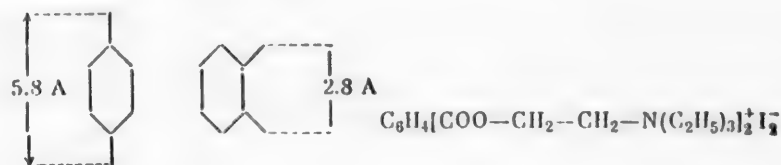
First Leningrad Medical Institute

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10, pp. 3196-3202,

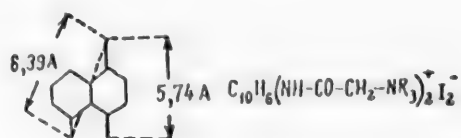
October, 1960

Original article submitted October 8, 1959

In recent years chemists who have synthesized medicinal preparations have devoted much attention to compounds which contain two quaternary ammonium groups in the molecule. Great significance has been attached to long chains which contain these quaternary ammonium groups. With change in chain length the pharmacological properties of the compounds change. Thus, if the chain consists of 5-7 atoms [1, 2] there are often gangliolytic properties; with increase in the chain to 9-12 atoms, as a rule, there are curare-like actions [3, 4], and if the chain consists of 10-14 atoms, the compounds sometimes acquire anticholinesterase activity (see, for example [5]). However, it often happens that these properties in one substance overlap each other, and usually then one of the properties predominates. Thus, for example, esters of para- and ortho-phthalic acids and triethylhydroxyethyl ammonium iodide have a curare-like action while in strong degree they show an anticholinesterase action. It has been shown that the para isomer of this ester selectively blocks a true cholinesterase, and the ortho isomer a pseudo one. This specificity of action is apparently explained by the difference in distance between the ester carbon (fixed by the rigidity of the benzene ring) in the ortho- and para-isomers. This difference is about 3 Å.

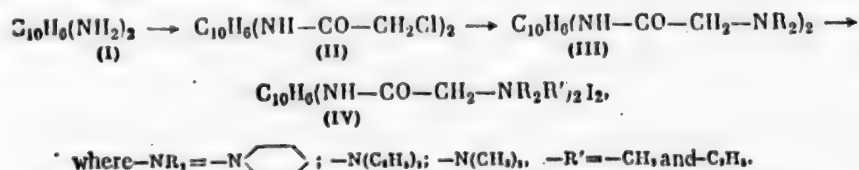


We have decided to synthesize and study substituted diacetyl derivatives of 1,4- and 1,5-naphthylene-diamines which contain quaternary ammonium groups in the acetyl portions. In this case, both in the 1,4- and the 1,5-isomers, the quaternary ammonium groups are found in chains of ten atoms. The difference in distance between the fixed NH groups in these isomers is 0.65 Å.



Pharmacologic study should establish whether the synthesized preparations have curare-like and anti-cholinesterase actions; in the presence of the latter it would be of interest to determine whether the isomeric compounds of the 1,4- and 1,5-naphthylenediamines have specific action on pseudo- and true cholinesterases.



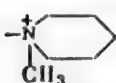
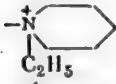
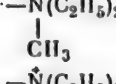
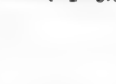
As starting substances for the synthesis of our compounds we used 1,4- and 1,5-naphthylenediamines. The syntheses were carried out by the following scheme:



The isomeric bis-chloroacetyl derivatives (II) were obtained by heating the corresponding naphthylene-diamine (I) with chloroacetyl chloride without a solvent. From the bis-chloroacetyl derivative (II) by the action of the corresponding amine we obtained bis-piperidine, bis-diethylamine, and bis-dimethylamine bases of the isomeric 1,4- and 1,5-naphthylenediamine derivatives (III) which by treatment with CH_3I or $\text{C}_2\text{H}_5\text{I}$ were then converted to the dimethiodides and diethiodides (IV). Eight of these compounds were chosen for pharmacological study*. It was shown that all the compounds have definite curare-like activity, but show in much greater measure anticholinesterase activity. This was studied with respect both to true and pseudo cholinesterases. The results of the pharmacological study are given in Table 1, which shows that specificity of the preparations for true and pseudo-cholinesterases in some cases reaches 1000.

TABLE 1

Weight Concentrations of Preparations Causing 50% Inhibition of Cholinesterases

R	 $\text{NH}-\text{CO}-\text{CH}_2-\text{R}$ $\text{NH}-\text{CO}-\text{CH}_2-\text{R}$ 2I		 $\text{NH}-\text{CO}-\text{CH}_2-\text{R}$ $\text{NH}-\text{CO}-\text{CH}_2-\text{R}$ 2I	
	True cholinesterase	Pseudo-cholinesterase	True cholinesterase	Pseudo-cholinesterase
	$4 \cdot 10^{-6}$	$1.5 \cdot 10^{-6}$	$9 \cdot 10^{-6}$	$5.6 \cdot 10^{-7}$
	$4 \cdot 10^{-7}$	$4 \cdot 10^{-6}$	$2.5 \cdot 10^{-5}$	$3 \cdot 10^{-8}$
	$1 \cdot 10^{-5}$	$5 \cdot 10^{-5}$	$2 \cdot 10^{-4}$	$3 \cdot 10^{-7}$
	$3.5 \cdot 10^{-6}$	$2.5 \cdot 10^{-5}$	$6.5 \cdot 10^{-5}$	$2.5 \cdot 10^{-6}$


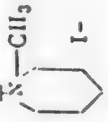

EXPERIMENTAL

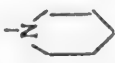
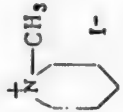
Preparation of bis-(chloroacetyl-amino)-naphthalenes of the 1,5 and 1,4 series. We boiled 1.5 g (0.01 mole) of the corresponding naphthylenediamine for 10-15 minutes with an excess of chloroacetyl chlorides without a solvent. The reaction mixture was cooled to room temperature, the excess chloroacetyl chloride was removed by treatment with alcohol, and the resulting precipitate was filtered off, washed 2-3 times with alcohol and ether, and dried. The yield was almost quantitative (Table 2). The resulting bis-chloroacetylaminonaphtha-

* We take this opportunity to express our thanks to A. V. Val'dman, M. Ya. Mikhel'son, N. K. Frumentov, and M. G. Bondarev who carried out the pharmacological study.

TABLE 2



No.	R	Calculated, %				Found, %				Yield, %	M. p.	Solubility
		C	H	N	Hal	C	H	N	Hal			
1,5-Naphthylenediamine derivatives												
1	Cl	54.03	3.59	9.00	22.83	54.66, 54.69	4.26, 4.09	9.03, 8.94	22.73, 22.48	96	300° (decomp.)	Insoluble in known solvents
2		70.58	7.94	13.70	—	71.32, 71.12	7.80, 7.73	13.52, 13.48	—	99.2	198—200	C_2H_5OH , CH_3COCH_3 , CH_3NO_2
3		—	—	8.09	36.70	—	—	8.24, 8.25	37.08, 36.88	88	226—227	H_2O (1 : 400) in the cold
4		—	—	7.77	35.27	—	—	7.45, 7.66	35.42, 35.55	89	222—224	Same
5	$-N(C_2H_5)_2$	68.75	8.33	14.58	—	69.05, 69.11	8.21, 7.64	14.90, 14.82	—	80	115—116	C_2H_5OH , CH_3COCH_3 , C_6H_6
6	$-\dot{N}(C_2H_5)_2$ $\quad $ $\quad C_2H_5$	—	—	8.38	38.02	—	—	8.04, 8.13	38.30, 37.95	70	213—214	C_2H_5OH , H_2O (1 : 80) in the cold
7	$-\dot{N}(C_2H_5)_2$ $\quad $ $\quad I$	—	—	8.04	36.49	—	—	8.04, 8.26	36.93, 36.52	90	215—216	H_2O (1 : 200) in the cold

No.	R	Calculated, %				Found, %				Yield, %	M. p.	Solubility
		C	H	N	Hal	C	H	N	Hal			
8	$-\text{N}(\text{CH}_3)_2$	65.85	7.31	17.07	—	65.36, 65.38	7.73, 7.78	16.97, 16.78	—	50	149—151	H_2O , $\text{C}_2\text{H}_5\text{OH}$
9	$-\dot{\text{N}}(\text{CH}_3)_2$ I ⁻	—	—	9.15	—	—	—	8.91, 9.27	—	70	243—245	H_2O
10	$-\dot{\text{N}}(\text{CH}_3)_2$ C ₂ H ₅ I ⁻	—	—	8.75	—	—	—	8.84, 8.98	—	50	215—216	H_2O , $\text{C}_2\text{H}_5\text{OH}$
1,4-Naphthylenediamine derivatives												
11	Cl	—	—	—	—	—	—	—	—	95	300° (decomp.)	Insoluble in known solvents
12		70.58	7.84	13.70	—	70.60, 70.72	8.02, 7.73	13.43, 13.69	—	90	144	$\text{C}_2\text{H}_5\text{OH}$, CH_3COCH_3
13	 I ⁻	—	—	8.09	—	—	—	7.82, 7.97	—	99	220—222	H_2O (1:400) in the cold $\text{C}_2\text{H}_5\text{OH}$

No.	R	Calculated, %				Found, %				Yield, %	M. p.	Solubility
		C	H	N	Hal	C	H	N	Hal			
14	$\text{K}^+ \text{C}_2\text{H}_5 \text{I}^-$	—	—	7.77	—	—	—	7.51, 7.47	—	90	207—209	H ₂ O (1:400) in the cold
15	$-\text{N}(\text{C}_2\text{H}_5)_2$	68.75	8.33	14.58	—	—	—	—	—	—	—	—
16	$-\text{N}(\text{C}_2\text{H}_5)_2$ CH ₃ I ⁻	—	—	8.38	38.02	—	—	8.16, 8.39	38.16, 37.74	70	185—187	H ₂ O (1:400) in the cold
17	$-\text{N}(\text{C}_2\text{H}_5)_2$	—	—	8.04	36.49	—	—	7.92, 8.17	36.93, 36.75	65	124—127	The same
18	$-\text{N}(\text{CH}_3)_2$	—	—	—	—	—	—	—	—	—	—	C ₂ H ₅ OH, CH ₃ COCH ₃ , ether
19	$-\text{N}(\text{CH}_3)_3$	—	—	9.15	—	—	—	—	—	—	—	—
20	$-\text{N}(\text{CH}_3)_2$ C ₂ H ₅ I ⁻	—	—	8.75	—	—	—	8.49, 8.48	—	50	203—204	C ₂ H ₅ OH

lenes (both 1,4- and 1,5-) were practically insoluble in ordinary organic solvents and so for further treatment they were used without recrystallization.

Amination of the bis-(chloroacetyl-amino)-naphthalenes. As the aminating agents we used piperidine, diethylamine, and a 36% aqueous solution of dimethylamine.

a) A mixture of 1 g (0.003 mole) of 1,5-bis-(chloroacetyl-amino)-naphthalene and 10 ml of piperidine was boiled for 10-12 minutes. At first there was almost complete solution, but then the reaction mixture quickly solidified. To the cooled reaction mixture was added 50 ml of water. The precipitate of 1,5-bis-(piperidinoacetyl-amino)-naphthalene (No. 2, Table 2) was filtered off and washed with water to disappearance of piperidine odor, dried, and recrystallized from alcohol. In an analogous way we obtained the 1,4-isomer (No. 12, Table 2) which was recrystallized from aqueous alcohol (1 : 1).

b) A mixture of 1 g (0.003 mole) of 1,5-bis-chloroacetylaminonaphthalene (No. 1, Table 2) and 10-12 ml of diethylamine was placed in a sealed ampule which was heated for 5-7 hours on a boiling water bath. The contents of the ampule were poured into water. The precipitate of 1,5-bis-(diethylaminoacetyl-amino)-naphthalene was filtered off, carefully washed with water to remove the hydrochloride of diethylamine, dried, and recrystallized from aqueous alcohol (1 : 1). In the same way we obtained the 1,4-isomer, and also the bis-dimethylamine analog. These bases were purified as follows: The contents of the ampule were poured into water and the water solution was treated with ether. After evaporation of the ether there remained a semiliquid mass which was used in the following reaction without purification.

Preparation of dimethiodides and diethiodides of the 1,4- and 1,5-naphthylenediamine diacetyl derivatives.

a) Four g (0.001 mole) of base No. 2 or the corresponding base No. 12 (Table 2) was dissolved in the cold in a minimum amount of acetone and to the solution was added CH_3I (10% excess). On the next day the reaction product was filtered, washed with acetone, and dried.

b) The reaction of bases No. 5, 8, 15, 18 (Table 2) with CH_3I was carried out in a sealed ampule on a boiling water bath for 5-7 hours. The ampule was opened, the precipitate was filtered off, washed with acetone, and dried.

The reaction of base No. 2 (Table 2) with $\text{C}_2\text{H}_5\text{I}$ was carried out in the cold (see process a). The reaction of bases No. 5, 8, 12, 15, 18 (Table 2) with $\text{C}_2\text{H}_5\text{I}$ was carried out in an ampule (see process b).

The resulting dimethiodides and diethiodides were purified as follows: Nos. 3, 4, 7, 9 were crystallized from a minimum amount of water; Nos. 6, 10, 13, 14, 16, 17, 19, 20 from alcohol.

SUMMARY

1. We have synthesized a series of substituted diacetyl derivatives of 1,4- and 1,5-naphthylenediamines which contain two quaternary ammonium groups in the acetyl portions.
2. We have shown that they all have marked curare-like, and also considerable anticholinesterase action.
3. We have studied the anticholinesterase action of these compounds and shown that all the derivatives of 1,4-naphthylenediamine selectively block the pseudo-cholinesterases, and almost all the derivatives of 1,5-naphthylenediamine block the true cholinesterases. The specificity of action of the 1,4- and the corresponding 1,5-naphthylenediamines is evidently related to the difference in distance between the amino groups in the 1,4- and 1,5-naphthylenediamines. These distances differ from each other by 0.65 Å.

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ACYLATION OF STEROID ALCOHOLS BY KETENE

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pp. 3203-3204, October, 1960

Original article submitted July 22, 1959

The present work is a continuation of an investigation begun earlier [1] on the treatment of yeast sterols which are partially used in the vitamin industry.

According to the literature [2], yeast sterols are a complex mixture of ergosterol (about 50%) with other alcohols, especially derivatives of the allo-series of Δ^7 - and Δ^8 -steroids. Ergosterol is widely used for the production of calciferol, progesterone, 11-corticosteroids, etc., while the "accompanying sterols" obtained in its isolation are waste products.

It was interesting to study some reactions of the "accompanying sterols" to see if a more rational use could be found, based on them, for the yeast steroids. One of such reactions is the protection of the hydroxyl group on C_3 by acylating it with ketene.

As is known, acylation reactions in a number of steroid alcohols have been well studied, using the accepted classical process which consists in treatment of the sterol with 20 times the amount of acetic anhydride with boiling. Among recent works there are interesting reports of acylation with mixtures of CH_3COOH and $(\text{CH}_3\text{CO})_2\text{O}$ in the presence of $p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_3\text{H}$ [3], the protection of the C_3 hydroxyl group by direct formylation [4], acylation of steroid alcohols by diacylamide acids [5], and others.

For the identification of the resulting substances with acetates of the "accompanying sterols" which were obtained according to [7] the products were twice recrystallized from alcohol, and in them was determined the content of acetate, the melting point, and we also took the infrared spectra in the region $1300\text{-}1800\text{ cm}^{-1}$. The source of the infrared radiation was a globe, and the determination was carried out on an IKS-12 spectrometer with an NaCl prism. For graduation of the apparatus we used the normal values recommended in the study [8].

The results of spectral analysis confirmed the identity of both products of acylation; the absorption band at 1739 cm^{-1} according to [9] is characteristic for sterol acetates.

Substance	Acetate Content, %	M. P.	Absorption maxima (in cm^{-1})
"Accompanying sterols". Acetates prepared with		138-146°	1380, 1419, 1480, 1622
a) ketene	99.6	91-98	1377, 1423, 1479, 1638, 1739
b) acetic anhydride	99.8	92-99	1377, 1422, 1480, 1636, 1739

Using ketene we tend to carry out the reaction under milder conditions, which would permit an increased yield of acetates. Preliminary experiments showed that sterols are well acylated by ketene in solutions in nonpolar solvents (benzene, xylene) even at ordinary temperature.

EXPERIMENTAL

The starting raw material consisted of the "accompanying sterols", the industrial wastes from the preparation of ergosterol in the Leningrad Vitamin Factory No. 2. Fifty g of crude sterols was dissolved by boiling in 300 ml of 96% alcohol; the solution was filtered hot and left for crystallization. The crystals which separated were filtered and dried in a vacuum at 50-60°. We obtained 36 g of a light cream colored substance with m. p. 138-146°.

Acylation was carried out with ketene obtained by pyrolysis of acetone [6] by passing it through a porcelain tube heated to 650-700° over pieces of quartz glass (yield of ketene 50%).

In a round bottomed, three necked flask (100 ml) fitted with a condenser, thermometer, and bubbler we placed 5 g of purified sterols and 10 ml of dry xylene. The mixture was heated to full melting of the crystals, and ketene obtained from 75 ml of acetone was passed into the melt at 85-90°. The duration of passing ketene was 15 minutes. The reaction product was recrystallized from 50 ml of alcohol and dried in a vacuum at 50-60°. We obtained 5.12 g of a white substance with an acetate content of 97.1% (calculated on an average molecular weight of 425).

SUMMARY

1. We have carried out and studied the over-all acetylation by ketene of Δ^7 - and Δ^8 -sterols from bakers yeast.
2. We have showed that the use of ketene as an acylating agent does not affect the nature of the yeast sterols and considerably simplifies their acylation and keeps a very high yield.
3. We have given the infrared spectrum of the starting sterols and their acetates in the region 1300-1800 cm^{-1} .

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THE SYNTHESIS OF NEW HOMOLOGS OF CYCLOPENTADIENE

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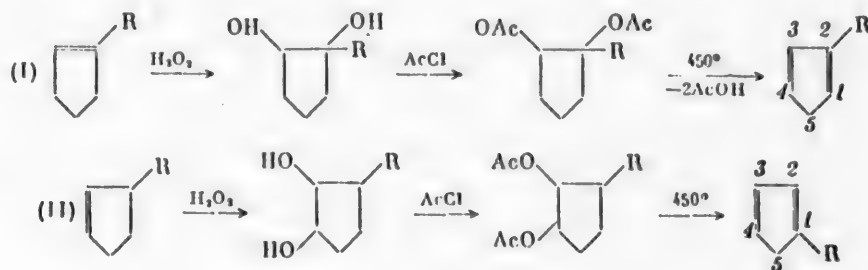
Original article submitted November 30, 1959

The great interest in the hydrocarbons of the cyclopentadiene series is explained by their high chemical activity. However, the chemistry of the homologs of cyclopentadiene in distinction from that of cyclopentadiene itself is almost unstudied, because of their slight availability.

One of the methods of synthesis of cyclopentadiene homologs is the thermal decomposition of alkylcyclopentenediol diacetates, which in their turn can be obtained by oxidation of alkylcyclopentenenes. This method of synthesis is somewhat long, but is desirable, since it does not give side products [1, 2]. Another method of obtaining homologs of cyclopentadiene is the dehydrobromination of dibromocyclopentanes [3]; but this method requires further improvement: the preparation by this method of cyclopentadiene and methylcyclopentadiene gave insufficiently pure products and their yield was small.

Using the ability of cyclopentadiene to give a metalloorganic derivative, for example potassium cyclopentadiene, we can introduce alkyl or aryl radicals in the cyclopentadiene ring. However, this method results only in obtaining cyclopentadiene hydrocarbons with substituents on the CH_2 group. Thus were synthesized homologs of cyclopentadiene [4] with substituents $\text{C}_1\text{-C}_4$ in position 5, and also gem-substituted cyclopentadienes [5, 6].

The basic problem of the present work was the synthesis of undescribed homologs of cyclopentadiene with alkyl substituents in positions 1 and 2. The synthesis was carried out in three steps according to schemes (I) or (II).



Since none of these steps in preparing homologs of cyclopentadiene are accompanied by isomerization reactions, then, starting from known structures of cyclopentenenes we can obtain alkylcyclopentadienes of definite structure. Thus, for example, for 1-alkyl-1-cyclopentenenes it is possible to go to 2-alkylcyclopentadienes (scheme I), while from 2-alkyl-1-cyclopentenenes are obtained homologs of cyclopentadiene with alkyl substituents in position 1 (scheme II).

Thus we have synthesized for the first time 1-methyl-, 2-ethyl-, and 2-n-propylcyclopentadienes.

EXPERIMENTAL

1-Methyl 1,3-cyclopentadiene was synthesized from 2-methyl-1-cyclopentene which was obtained in fractionation of the products of the contact reaction of cyclohexanol with aluminum oxide at 450°; in the products along with 1-methyl-1-cyclopentene [7] we found 2-methyl-1-cyclopentene (b. p. 65° at 759 mm, n_D^{20} 1.4200, d_4^{20} 0.7709).

To 115 g of this hydrocarbon dissolved in 575 ml of formic acid we added gradually with stirring 190 ml of 30% hydrogen peroxide; the temperature of the reaction mixture did not exceed 30°. The resulting 1-methylcyclopentane-2,3-diol was extracted with ether and distilled in a vacuum; b. p. 127° (13 mm), n_D^{20} 1.4760 and d_4^{20} 1.0726. Yield 94.8 g (58%).

To obtain the diacetate we added gradually to a mixture of 90.1 g of glycol, 246 ml of ether, and 360 ml of dimethylaniline, an amount of 177 g of acetyl chloride; the reaction mixture was boiled under reflux for 5 hours, the reaction product was treated with water and then with dilute (1 : 1) hydrochloric acid, washed with 10% soda solution, then with water again, and after drying with calcium chloride was distilled from a Claisen flask in a vacuum. We obtained 88 g, or 73%, of 1-methylcyclopentane-2,3-diol diacetate: b. p. 120° (20 mm), n_D^{20} 1.4430 and d_4^{20} 1.0586.

The diacetate was pyrolyzed at 450° in a quartz tube filled with pieces of broken quartz. The product was supplied to the reaction zone at a rate of 0.2 hour⁻¹ in a stream of nitrogen. The pyrolyzate was neutralized with a soda solution, washed with water, and dried with calcium chloride. After distillation from a rectifying column and then through a column with 30 theoretical plates we obtained 14.5 g, or 33%, of 1-methyl-1,3-cyclopentadiene;

b. p. 73.5-74° (749 mm), n_D^{20} 1.4410, d_4^{20} 0.8053, MR_D 26.26. $C_6H_8F_2$. Calculated: 26.77.

Found %: C 89.68; H 10.01. C_6H_8 . Calculated %: C 89.92; H 10.08.

The combination light scattering spectrum* of this hydrocarbon was characterized by the following frequencies in cm⁻¹ (the intensity of the lines given on a 10 point visual scale): 235 (2w), 273 (0), 323 (3w), 360 (1), 553 (1), 615 (4), 818 (1w), 870 (2), 899 (3), 927 (4), 980 (0), 1005 (2w), 1083 (2w), 1101 (6), 1169 (0), 1195 (3), 1238 (2), 1292 (1), 1356 (5w), 1380 (6), 1450 (3w), 1526 (10), 1577 (0), 1606 (3w), 1634 (1), 1662 (1), 2877 (10), 2915 (6), 2962 (1), 3056 (2), 3087 (5).

2-Ethyl-1,3-cyclopentadiene was synthesized in the same way from 1-ethyl-1-cyclopentene (b. p. 106-107° at 750 mm, n_D^{20} 1.4405, d_4^{20} 0.7976) obtained by the Grignard reaction from ethyl bromide and cyclopentanone followed by dehydrogenation of the 1-ethyl-1-cyclopentanol. As a result of oxidation of 105 g of 1-ethyl-1-cyclopentene we isolated 89.3 g, or 63%, of 1-ethylcyclopentane-1,2-diol with b. p. 130-132° (15 mm), n_D^{20} 1.4770 and d_4^{20} 1.0775. By decomposition of 79 g of 1-ethylcyclopentane-1,2-diol acetate (b. p. 125-126° at 10 mm, n_D^{20} 1.4467, d_4^{20} 1.0532) and treatment of the pyrolysis product we obtained 13.5 g, or 29%, of ethylcyclopentadiene which was evidently the β -isomer;

b. p. 104-105° (748 mm), n_D^{20} 1.4625, d_4^{20} 0.8231, MR_D 31.46. $C_7H_{10}F_2$. Calculated: 31.38.

Found %: C 88.87; H 10.71. C_7H_{10} . Calculated %: C 89.29; H 10.71.

The combination scattering spectrum of this hydrocarbon was characterized by the following frequencies (in cm⁻¹): 412 (1), 478 (1), 622 (2w), 810 (2w), 870 (1), 895 (2w), 928 (3w), 950 (1w), 1002 (1w), 1062 (1), 1085 (1), 1105 (7), 1177 (1), 1200 (3), 1224 (0), 1295 (1), 1327 (1w), 1363 (3w), 1385 (5w), 1448 (3), 1524 (10), 1580 (4), 1602 (1), 1632 (2), 1655 (4), 1672 (1), 2845 (1), 2906 (3w), 2935 (4), 2969 (5), 3065 (3w), 3088 (5).

1-n-Propyl-1,3-cyclopentadiene was synthesized in an analogous way; from 102 g of 1-n-propyl-1-cyclopentene (b. p. 130.5° at 735 mm, n_D^{20} 1.4450, d_4^{20} 0.8025) we obtained 81.8 g, or 61%, of 1-n-propylcyclopentane-1,2-diol with b. p. 135° (20 mm), n_D^{20} 1.4780, d_4^{20} 1.0507. The diacetate of 1-n-propylcyclopentane-1,2-diol (b. p. 135-136° at 18 mm, n_D^{20} 1.4490, d_4^{20} 1.0383) was decomposed pyrolytically and converted to 2-n-propyl-

*The spectral analysis was carried out by Yu. P. Egorov and G. K. Gaivoronskaya, to whom we express our thanks.

** w = wide, n = narrow, d = doublet.

1,3-cyclopentadiene. After distillation through a column we collected 15.1 g, or 36%;

b. p. 135-136° (745 mm), n_D^{20} 1.4680, d_4^{20} 0.8288, MR_D 36.26. $C_8H_{12}F_2$. Calculated: 36.00.

Found %: C 88.54; H 10.90. C_8H_{12} . Calculated %: C 88.80; H 11.20.

The combination scattering spectrum of 2-n-propyl-1,3-cyclopentadiene gave the following frequencies (in cm^{-1}): 437 (1), 507 (0w), 628 (0w), 853 (0), 887 (0), 913 (1), 930 (1), 952 (3), 1031 (2w), 1098 (5w), 1120 (2), 1295 (4w), 1348 (1), 1382 (4w), 1452 (3d), 1523 (8), 1580 (5), 1603 (3), 1653 (10), 2846 (3), 2875 (7), 2905 (2), 2934 (4), 2960 (3), 3060 (3), 3088 (4).

In all these homologs of cyclopentadiene we found the stable lines 1100, 1523, 1580, 1603, 1654, 3060, 3088 cm^{-1} . This shows the related nature of all the substances and also the presence in them of the cyclopentadiene ring (frequencies 1100 and 1523 cm^{-1}).

SUMMARY

We have synthesized the undescribed 1-methyl-1,3-cyclopentadiene, 2-ethyl-1,3-cyclopentadiene, and 2-n-propyl-1,3-cyclopentadiene.

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* Original Russian pagination. See C. B. translation.

THE SYNTHESIS OF HYDROCARBONS

LXXVI. CYCLOHEXANES WITH THREE QUATERNARY CARBON ATOMS IN THE RING

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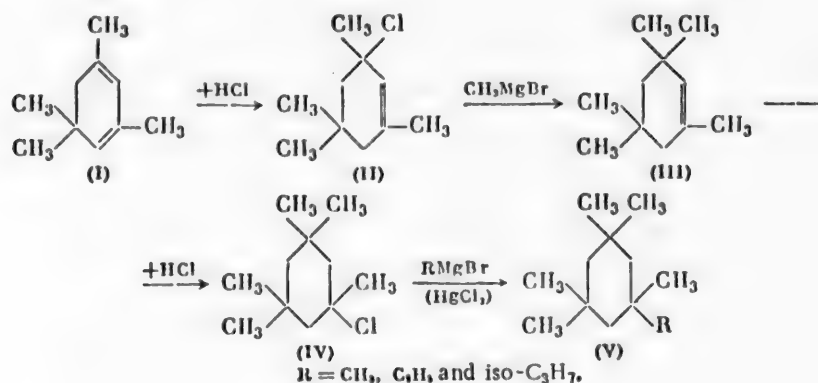
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Earlier [2, 3] we described a path for the synthesis of cyclohexane hydrocarbons with one and two quaternary carbon atoms* on the basis of 1,3-dimethyl-1,3-cyclohexadiene. In the present work we describe a general method for the synthesis of cyclohexane hydrocarbons which contain three quaternary carbon atoms in the ring, separated by methylene groups**, 1,3,3,5,5-pentamethyl-1-alkylcyclohexanes.

For the synthesis of hydrocarbons with this structure the starting substance was a cyclohexadiene hydrocarbon which already contained one quaternary carbon atom, 1,1,3,5-tetramethyl-2,4-cyclohexadiene (I).

The synthesis was carried out by the following scheme.



The monohydrochlorinated derivative (II) of 1,1,3,5-tetramethyl-2,4-cyclohexadiene was a tertiary unsaturated chloride of the allyl type (which did not form the isomeric chloride by allyl rearrangement) and was reacted with methylmagnesium bromide. To the product of this reaction, 1,1,3,3,5-pentamethyl-4-cyclohexene, (III), was added hydrogen chloride; the resulting saturated tertiary chloride (IV) was reacted with alkyl magnesium bromide in the presence of a catalyst, mercuric chloride. The yield of 1,3,3,5,5-pentamethyl-1-alkylcyclohexanes (V) in this second Grignard-Wurtz reaction was 4-8%, since under the conditions of running the reaction most of the saturated tertiary chloride (IV) lost hydrogen chloride and reverted to the form of the starting pentamethylcyclohexene (III); the latter was again used for the synthesis of the cyclohexane hydrocarbon.

*As is known, cyclohexane hydrocarbons which contain quaternary carbon atoms in the ring occur in various petroleum fractions [1].

**Cyclohexanes with three quaternary carbon atoms have not been described in the literature.



Hexaalkylcyclohexanes with the Structure

General formula	R	Name	Setting temperature	B. p. (pressure in mm)	n_D^{20}	d_4^{20}	MRD		% Cen-tistokes	Found ^{••} , %	
							found	calculated		C	H
$C_{12}H_{24}$	CH_3	1,1,3,3,5,5-Hexamethylcyclohexane ^{••}	-13° (Crystals)	183-183.5° (750)	1.4460	0.8032	55.89	55.42	2.36	85.77, 85.63	14.38, 14.40
$C_{13}H_{26}$	C_2H_5	1,3,3,5,5-Pentamethyl-1-ethylcyclohexane	-80 (Glass)	201-201.6 (740)	1.4544	0.8173	60.45	60.03	2.78	85.60, 85.48	14.37, 14.50
$C_{14}H_{28}$	iso- C_3H_7	1,3,3,5,5-Pentamethyl-1-iso-propylcyclohexane	-70 (Glass)	222.9-223.7 (750)	1.4609	0.8301	64.93	64.65	4.27	85.58, 85.81	14.40, 14.24

[•]T. P. Surikova took part in the synthesis of this hydrocarbon.

^{••}Calculated %: C 85.64, H 14.36.

EXPERIMENTAL

1,1,3,5-Tetramethyl-2,4-cyclohexadiene (I) was obtained with a yield of 65% by the method of Kharasch and Tawney [4] by the reaction between isophorone (1,1,3-trimethyl-3-cyclohexen-5-one, b. p. 212-213° at 745 mm, n_D^{20} 1.4798, d_4^{20} 0.9235; obtained by the action of calcium carbide on acetone) and methyl magnesium bromide with later splitting out of water (potassium bisulfate) from the thus formed tertiary unsaturated alcohol. The diene hydrocarbon had the following constants.

B. p. 75-77° (45 mm), n_D^{20} 1.4712, d_4^{20} 0.8139. Literature data [4]: b. p. 24-25° (7 mm), n_D^{20} 1.4698, d_4^{20} 0.8152.

1,1,3,3,5-Pentamethyl-4-cyclohexene (III). Into 137 g (1 mole) of 1,1,3,5-tetramethyl-2,4-cyclohexadiene (I) with cooling with snow and salt was passed dry hydrogen chloride to a weight of 37 g. The resulting unsaturated tertiary chloride (II) (to avoid splitting hydrogen chloride from it) was rapidly diluted with ether and added with cooling by ice water to methylmagnesium bromide (36 g of magnesium, 400 ml of ether). On the next day the reaction mixture was boiled for three hours and decomposed by pouring onto ice with the addition of acetic acid. The residue obtained after distillation of the ether from the washed and dried ether extract was distilled over sodium and then fractionated on a column. Yield of 1,1,3,3,5-pentamethyl-4-cyclohexene 70 g (45%).

B. p. 161-162° (750 mm), n_D^{20} 1.4495, d_4^{20} 0.8020. Literature data [5]: b. p. 162.4-162.9° (760 mm), n_D^{20} 1.4490, d_4^{20} 0.8041.

1,3,3,5,5-Pentamethyl-1-alkylcyclohexanes (V). We shook 152 g (1 mole) of 1,1,3,3,5-pentamethyl-4-cyclohexene (III) for two days with hydrochloric acid saturated (when cooled with ice water) with hydrogen chloride. The resulting saturated tertiary chloride (IV) easily lost hydrogen chloride, and therefore immediately after washing it with water and drying, it was introduced at 12-15° into reaction with alkylmagnesium bromide (49 g of magnesium, 2 moles of alkyl bromide, and 500 ml of ether) to which had first been added mercuric chloride (8 g). On the next day the reaction mixture was boiled for three hours and decomposed with 2 N hydrochloric acid. The ether was distilled from the washed and dried ether extract; the residue was boiled for 0.5 hour over sodium and distilled. We collected a fraction of starting pentamethylcyclohexene (III) (about 80% of that introduced into the reaction) and the above mentioned fraction of 1,3,3,5,5-pentamethyl-1-alkylcyclohexane (V); the latter was shaken for about one hour with hot concentrated hydrochloric acid (for complete removal of possible admixtures of mercury organic compounds), washed free of acid, dried, distilled over sodium, and fractionated in a column (35 theoretical plates). The isolated saturated hydrocarbon (V) was further purified by chromatography over silica gel. Yield of 1,3,3,5,5-pentamethyl-1-alkylcyclohexanes (V) was 4-8% on the pentamethylcyclohexene (III) introduced into the reaction, or 20-40% on that used; the constants and data of analysis are given in the Table.

Judging by the combination scattering spectra, the synthesized hexaalkylcyclohexanes (V) do not contain admixtures of unsaturated hydrocarbons.

SUMMARY

1. We have worked out a method for the synthesis of cyclohexane hydrocarbons of a previously undescribed type, which contain three quaternary carbon atoms in the ring.

2. By this method we have synthesized 1,1,3,3,5,5-hexamethylcyclohexane, 1,3,3,5,5-pentamethyl-1-ethylcyclohexane, and 1,3,3,5,5-pentamethyl-1-isopropylcyclohexane.

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CYCLOPROPANES AND CYCLOBUTANES

XI. METHYLPHENYLCYCLOBUTANES

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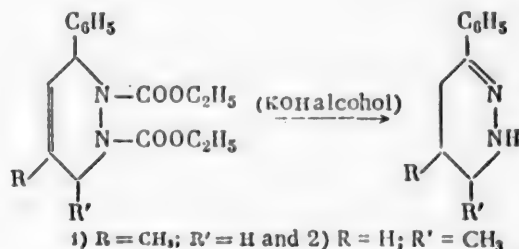
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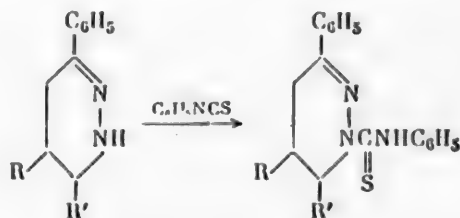
Original article submitted December 7, 1959

We have previously described the catalytic decomposition (in the presence of potassium hydroxide and platinum) of alkyl and aryltetrahydropyridazines. We have shown that the decomposition of aryltetrahydropyridazines can serve as a method for the synthesis of arylcyclobutanes [1-3]; we could not obtain alkylcyclobutanes in an analogous way [4].

In the present work we have studied the possibility of using the catalytic decomposition of alkylaryl-tetrahydropyridazines for the synthesis of alkylaryl-cyclobutanes. For this study we have used 5-methyl- and 6-methyl-3-phenyltetrahydropyridazines, obtained by hydrolysis of the adducts of the corresponding dienes with azodicarboxylic esters.

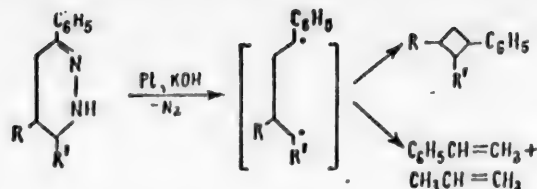


Methylphenyltetrahydropyridazines are unstable compounds which are rapidly oxidized in air; they were characterized in the form of their addition products with phenyl isothiocyanate.



This reaction showed at the same time the presence of one NH group in each of the tetrahydropyridazines (and hence also the structure of the hydrolysis products as Δ^2 -tetrahydropyridazines [3]).

Catalytic decomposition of both methylphenyltetrahydropyridazines was carried out under the conditions which we used before [1-3] for the decomposition of the aryltetrahydropyridazines. We showed that in the reaction there is evolution of a gas which consists of nitrogen and propylene, and we obtained a mixture consisting of methylphenylcyclobutane and styrene.



Thus the decomposition of alkylaryl-tetrahydropyridazines occurs analogously to the decomposition of aryl- Δ^2 -tetrahydropyridazines, evolving nitrogen and forming an intermediate biradical which cyclizes into a cyclobutane with simultaneous splitting into two ethylene hydrocarbons.

The molar ratio (K) of the amount of methylphenylcyclobutane and styrene is determined by the corresponding amounts of nitrogen and propylene in the gas [3].

It was shown that the value of K depends on the position of the methyl group in the tetrahydropyridazine ring; in the case of 6-methyl-3-phenyl- Δ^2 -tetrahydropyridazine, $K=0.5$, and in the case of 5-methyl-3-tetrahydropyridazine, $K=3.0$.

Distillation of the cyclobutane hydrocarbons obtained in this way in a vacuum column (80 theoretical plates) showed that 1-methyl-2-phenylcyclobutane consists of a mixture of about equal amounts of cis- and trans-isomers, and 1-methyl-3-phenylcyclobutane contains 80% of the trans form. It should be noted that the fact of preferential formation of the trans-isomer has analogies in a number of dialkylcyclobutanes [5].

All the isomeric methylphenylcyclobutanes were studied by the method of combination light scattering; the spectra showed that the resulting hydrocarbons do not contain unsaturated impurities. The presence of the four member ring was confirmed by the characteristic frequencies in the region $912\text{--}950\text{ cm}^{-1}$.

EXPERIMENTAL

The starting dienes were obtained from the magnesium organic compounds by the method described for the synthesis of 1-phenyl-1,3-butadiene [6].

1-Phenyl-1,3-pentadiene (from cinnamaldehyde and ethylmagnesium bromide; yield 60%);

b. p. $93\text{--}95^\circ$ (8 mm), n_D^{20} 1.6103. Literature data [7]: b. p. $112\text{--}114.5^\circ$ (15 mm), n_D^{20} 1.6111.

2-Methyl-4-phenyl-1,3-butadiene (from benzalacetone and ethylmagnesium bromide; the yield varied from 15 to 65%);

b. p. $100\text{--}105^\circ$ (8 mm); m. p. $35\text{--}36^\circ$. Literature data [8]: m. p. 37° .

Adducts of azodicarboxylic esters with both dienes (1,2-dicarbethoxy- Δ^4 -tetrahydropyridazines) were obtained by mixing at 0° solutions of equivalent amounts of azodicarboxylic esters and dienes in anhydrous benzene or ether. The mixtures were kept for about three hours at 0° and then stood overnight at room temperature. After the solvent had been distilled off, the reaction products were isolated by vacuum distillation.

6-Methyl-3-phenyl-1,2-dicarbethoxy- Δ^4 -tetrahydropyridazine (from 1-phenyl-1,3-pentadiene; yield 80%);

b. p. $194\text{--}195^\circ$ (8 mm), m. p. $74.5\text{--}75^\circ$. Literature data [9]: m. p. $75\text{--}76^\circ$.

Found %: N 8.82, 8.88. $C_{17}H_{22}O_4N_2$. Calculated %: N 8.80.

5-Methyl-3-phenyl-1,2-dicarbethoxy- Δ^4 -tetrahydropyridazine (from 2-methyl-4-phenyl-1,3-butadiene; yield 35%);

b. p. $192\text{--}193^\circ$ (11 mm), m. p. $62\text{--}62.5^\circ$.

Found %: N 8.54, 8.74. $C_{17}H_{22}O_4N_2$. Calculated %: N 8.80.

Methylphenyl- Δ^2 -tetrahydropyridazine was obtained by hydrolysis and simultaneous decarboxylation of the adduct by the method described in the previous work [2, 3].

6-Methyl-3-phenyl- Δ^2 -tetrahydropyridazine (yield 60%), b. p. 160-163° (8 mm), m. p. 43°.

5-Methyl-3-phenyl- Δ^2 -tetrahydropyridazine (yield 65%), b. p. 150-155° (8 mm).

Addition of methylphenyltetrahydropyridazines to phenylisothiocyanate (taken in excess [10]), that is, obtaining the anilide of the corresponding thiocarboxylic acid, took place with heating. At the end of the reaction the mixture was cooled and the resulting thick oil was washed with ligroin and 50% alcohol; the residue was recrystallized from 95% alcohol.

Anilide of 6-methyl-3-phenyl- Δ^2 -tetrahydropyridazine-1-thiocarboxylic acid, m. p. 105-105.5°.

Found %: N 13.28, 13.44. $C_{18}H_{19}N_3S$. Calculated %: N 13.58.

Anilide of 5-methyl-3-phenyl- Δ^2 -tetrahydropyridazine-1-thiocarboxylic acid, m. p. 131-131.5°.

Found %: N 13.52, 13.52. $C_{18}H_{19}N_3S$. Calculated %: N 13.58.

Catalytic decomposition of the methylphenyl- Δ^2 -tetrahydropyridazines was carried out by heating a mixture of 0.1 mole of tetrahydropyridazine with 0.2-0.3 g of potassium hydroxide and 0.5 g of platinum catalyst. Isolation of the liquid reaction products and analysis of the evolved gases were carried out by the methods previously described [2, 3].

Styrene was distilled from each catalyzate, the residue was heated with sodium for about three hours and vacuum distilled.

Decomposition of 6-methyl-3-phenyl- Δ^2 -tetrahydropyridazine.

Composition of the gases: propylene 41%, nitrogen 59%.

Styrene: yield 30%, b. p. 64-66° (50 mm), n_D^{20} 1.5460.

1-Methyl-2-phenylcyclobutane (mixture of cis- and trans-isomers); yield 12-15%; b. p. 70-75° (7 mm), n_D^{20} 1.5185.

Found %: C 90.26, 90.35; H 9.82, 9.84. $C_{11}H_{14}$. Calculated %: C 90.35; H 9.65.

Decomposition of 5-methyl-3-phenyl- Δ^2 -tetrahydropyridazine.

Composition of gases: propylene 20%, nitrogen 80%.

Styrene: yield 10%; b. p. 64-66° (50 mm), n_D^{20} 1.5455.

1-Methyl-3-phenylcyclobutane (mixture of cis- and trans-isomers); yield 27%, b. p. 72-80° (7 mm), n_D^{20} 1.5170.

Found %: C 90.31, 90.18; H 9.70, 9.65. $C_{11}H_{14}$. Calculated %: C 90.35; H 9.65.

After accumulation of a sufficient amount of isomers of the methylphenylcyclobutanes, each of them was distilled on a column* with 80 theoretical plates to separate the geometrical isomers.

The isomers with the higher constants were assigned the cis-configuration in accord with the Auwers-Skita rule. The constants of the geometrical isomers are given in the table.

SUMMARY

1. We have showed that the method of obtaining arylcyclobutanes by catalytic decomposition of tetrahydropyridazines can be used for the synthesis of alkylaryl cyclobutanes.

2. We have synthesized and separated into geometrical isomers 1-methyl-2-phenylcyclobutane and 1-methyl-3-phenylcyclobutane.

*1-Methyl-3-phenylcyclobutane was first purified from unsaturated impurities by heating with 2,4-dinitrobenzenesulfonyl chloride [11].

Methylphenylcyclobutanes

Name	B. p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D^{20}	EM_D
1-Methyl-2-phenylcyclobutane (cis)	95—95.2° (15)	1.5210	0.9280	47.99	0.19
1-Methyl-2-phenylcyclobutane (trans)	91.9—92.0 (15)	1.5140	0.9136	48.18	0.38
1-Methyl-3-phenylcyclobutane (cis)	103—103.5 (15)	1.5238	0.9302	48.09	0.29
1-Methyl-3-phenylcyclobutane (trans)	97.4—97.6 (15)	1.5150	0.9109	48.42	0.62

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STUDIES IN THE FURAN SERIES

VIII. TETRAMETHYLFURAN IN THE DIENE REACTION SYNTHESIS

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pp. 3214-3217, October, 1960

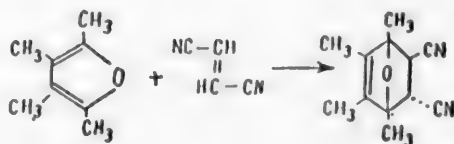
Original article submitted November 20, 1959

Furan and its homologs undergo the diene synthesis only with very active dienophils which have electron acceptor substituents on each of the carbon atoms attached to the double bond [1]. However, furan does not react even with such sufficiently active dienophils as phenyl- β -benzoylvinyl sulfone [2], bis-phenylsulfonylethylene [3], quinone [4], and dibenzoylethylene [5]. Furan derivatives which have electron acceptor substituents in the ring, furfural, pyromucic acid, nitrovinylfuran, etc. [6], do not give the diene synthesis even with maleic anhydride which is one of the strongest dienophils.

All of these results can be explained from the point of view of the ionic mechanism of the diene synthesis, according to which the reaction begins with formation of an ionic complex by transfer of electrons from the diene to the dienophile to such an extent that this electron transfer is compensated by the electrostatic interaction [7, 8]. Furan itself has a weak electron donor character and in order to react requires a dienophile with a clearly demonstrated electron unsaturated double bond, such as is found in the most active dienophils. If, in the dienophile, there is a substituent on the double bond which has the character of an electron donor, then the electron unsaturated double bond is not sufficient for its reaction with furan [5, 9]. On the other hand, in the presence of an electron acceptor group as the substituent in the furan ring, the latter has such a small electron density that for this reason the diene synthesis does not occur in these compounds.

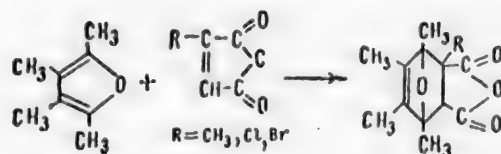
The presence in the furan ring of alkyl substituents which increase the electron density in the ring should make possible the occurrence of the diene synthesis. Hence it follows that completely alkylated furans such as, for example, tetramethylfuran, should be more active in this reaction. A study of the behavior of tetramethylfuran in the diene synthesis is the purpose of the present work. We should note, however, that there are some examples of the diene synthesis reaction in the furan series which take place, evidently, not by the ionic mechanism. This includes the reaction of furan with ethylene [10], vinylene carbonate [11], cyanallene [12], and with the active double bond in some bicyclic systems [9, 11]. However, the largest number of reactions of the diene synthesis in the furan series are well explained just from the point of view of the ionic mechanism.

It is known from the literature [13] that tetramethylfuran reacts with maleic anhydride with formation of the corresponding thermally stable adduct. We found that tetramethylfuran reacted energetically with fumaronitrile according to the scheme.



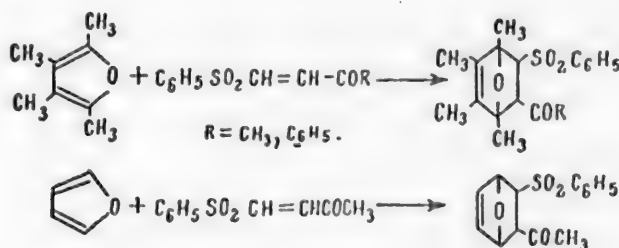
In studying the behavior of tetramethylfuran in the diene synthesis we felt it interesting to confirm qualitatively the difference in reactivity of tetramethylfuran and furan and to select those dienophils which would react with tetramethylfuran and would not react with furan.

We showed that tetramethylfuran reacts with methylmaleic anhydride with formation of a crystalline adduct while furan, 2-methylfuran, and 2,5-dimethylfuran do not react with this dienophile. Chloro- and bromomaleic anhydrides also give the corresponding adducts with tetramethylfuran.



However, phenylmaleic anhydride does not react with tetramethylfuran.

We also found that phenyl- β -benzoylvinyl sulfone, which does not react with furan [2], reacts with tetramethylfuran giving the corresponding crystalline adduct; phenyl- β -acetylvinyl sulfone also reacts with tetramethylfuran, but in distinction from phenyl- β -benzoylvinyl sulfone this dienophile also reacts with furan itself.



Thus, in the examples of these dienophils we have clearly shown that differences in reactivity of tetramethylfuran and furan are quite large.

Our numerous attempts to bring tetramethylfuran into the diene synthesis with dimethylmaleic anhydride, benzalmalonic ester, acrolein, methylisopropenyl ketone, acrylonitrile, and cinnamaldehyde did not give positive results. This indicates that tetramethylfuran, like furan, is not sufficiently reactive a diene to react with dienophils whose double bond is activated on only one side [14-16].

In this connection we should make the following remarks. In 1958 Wiehnhaus and Dässlep [17] reacted menthofuran with acrolein and crotonaldehyde, considering that in these cases there was a diene synthesis. However, it is known [15, 16] that in the presence of small amounts of impurities of an acid nature, α, β -unsaturated aldehydes and ketones react with furan and 2-methylfuran by a type of substitutive addition. Our observed negative result in the reaction of tetramethylfuran with acrolein forces us to consider the data of these authors carefully, since in the presence of the free α -position in the furan ring of menthofuran the reaction of substitutive addition should easily occur.

Hence a further investigation is required to establish the structure of the reaction product between acrolein and menthofuran.

EXPERIMENTAL

Trans-dinitrile of 3,4,5,6-tetramethyl-1,3,6-endooxo- Δ^4 -tetrahydrophthalic acid. One g of tetramethylfuran (b. p. 145-147°, n_D^{20} 1.4561 [10]) was mixed with a solution of 0.5 g of fumaronitrile in 8 ml of dioxane and at the end of the strong heating, was heated for 10 hours at 45°. The solvent was distilled off in a vacuum and the residue was recrystallized from aqueous alcohol. We obtained 1.4 g; m. p. 103°; white crystals.

Found %: C 71.13, 70.91; H 6.81, 6.88. $C_{12}H_{14}ON_2$. Calculated %: C 71.40; H 6.81.

Anhydride of cis-1,3,4,5,6-pentamethyl-1,3,6-endooxo- Δ^4 -tetrahydrophthalic acid. One g of tetramethylfuran in 2 ml of ether was mixed with 0.9 g of methylmaleic anhydride in 2 ml of ether. After a day the crystals

were filtered off (sometimes crystallization had to be induced). We obtained 1.6 g; m. p. 82° (from ether); white crystals.

Found %: C 65.93, 65.84; H 6.82, 6.77. $C_{13}H_{16}O_4$. Calculated %: C 66.12; H 6.77.

Anhydride of cis-1-chloro-3,4,5,6-tetramethyl-3,6-endooxo- Δ^4 -tetrahydrophthalic acid. We mixed 0.55 g of tetramethylfuran in 2 ml of ether and 0.5 g of chloromaleic anhydride in 2 ml of ether at -30°; the solution at once became a bright red which then changed to yellow. After standing a day at 20° the solvent was evaporated and the residue recrystallized from ether with activated charcoal. We obtained 0.5 g; m. p. 86-87°; white crystals. When kept the substance became pink and decomposed.

Found %: C 52.35, 52.20; H 5.39, 5.40; Cl 14.7. $C_{12}H_{13}O_4Cl$. Calculated %: C 52.45; H 5.49; Cl 15.1.

Anhydride of cis-1-bromo-3,4,5,6-tetramethyl-3,6-endooxo- Δ^4 -tetrahydrophthalic acid. We mixed 0.5 g of tetramethylfuran in 2 ml of ether and 0.5 g of freshly distilled bromomaleic anhydride in 2 ml of ether at -50°. The solution became red and then yellow. After standing for several days at 5° crystals precipitated, contaminated with tar. They were dissolved in ether, treated with activated charcoal, filtered, and to the brown filtrate ligroin was added dropwise to turbidity; the cloudiness was dissolved by addition of ether and the solvent was slowly evaporated. Crystals separated and were crystallized from a mixture of ether-ligroin. We obtained 0.4 g; m. p. 71-72°; white crystals which rapidly turned pink.

Found %: C 44.38, 44.48; H 4.63, 4.59. $C_{12}H_{13}O_4Br$. Calculated %: C 44.26; H 4.62.

3,4,5,6-Tetramethyl-3,6-endooxo-2-acetyl- Δ^4 -cyclohexenyl sulfone. We dissolved 0.4 g of phenyl- β -acetylvinyl sulfone in 0.5 g of tetramethylfuran. Reaction occurred with heating and the mixture quickly crystallized. We obtained 0.6 g; m. p. 97° (from anhydrous methanol); white needles.

Found %: C 64.57, 64.61; H 6.83, 6.85. $C_{18}H_{22}O_4S$. Calculated %: C 64.63; H 6.65.

3,6-Endooxo-2-acetyl- Δ^4 -cyclohexenylphenyl sulfone. We dissolved 0.2 g of phenyl- β -acetylvinyl sulfone in 1 ml of furan, allowed it to stand for 2 days at 20° and evaporated the excess furan. We obtained 0.26 g of adduct with m. p. 107° (from anhydrous methanol); white needles.

Found %: C 60.65, 60.50; H 5.35, 5.23. $C_{14}H_{14}O_4S$. Calculated %: C 60.42; H 5.07.

3,4,5,6-Tetramethyl-3,6-endooxo-2-benzoyl- Δ^4 -cyclohexenylphenyl sulfone. We added 0.7 g of tetramethylfuran in 0.5 ml of benzene to a solution of 1.3 g of phenyl- β -benzoylvinyl sulfone (m. p. 115°) in 10 ml of benzene and left it for three days. Then we evaporated the solvent almost dry in a vacuum and filtered the crystalline residue; it was washed on the filter with anhydrous methanol. After crystallization from anhydrous methanol we obtained 0.8 g. When heated, the adduct decomposed into its components and melted at 115° (the m. p. of phenyl- β -benzoylvinyl sulfone).

Found %: C 69.92; H 6.08. $C_{23}H_{24}O_4S$. Calculated %: C 69.67; H 6.10.

SUMMARY

1. Starting from the idea of the ionic mechanism for the course of the Diels-Alder synthesis in the furan series, we have showed that tetramethylfuran is a more active diene than furan. As confirmation of the qualitative differences in reactivity of tetramethylfuran and furan we have the positive result of the reaction of tetramethylfuran with methyl-, chloro-, and bromomaleic anhydrides and also with phenyl- β -benzoylvinyl sulfone, with which furan does not react.

2. Tetramethylfuran does not react with dienophiles whose double bond is activated on only one side, as occurs in the case of acrolein and acrylonitrile.

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STUDIES IN THE FURAN SERIES.

IX. SYNTHESIS OF 2,5-BIS(AMINOMETHYL)FURANS

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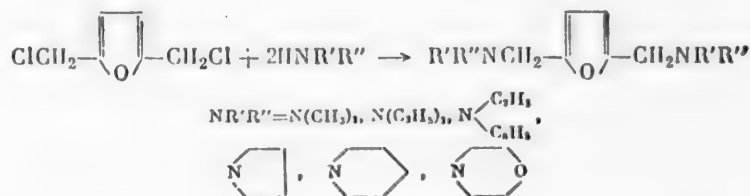
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pp. 3218-3220, October, 1960

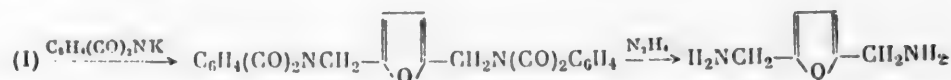
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The synthesis of symmetrical diamines of the furan series was recently described by Gill and Ing [1] who aminomethylated dimethylamine with dimethylfurfurylamine hydrochloride and obtained 2,5-bis(dimethylaminomethyl)furan (70% calculated on the reacting amine). A. L. Mndzhoyan and co-workers [2] carried out the synthesis of 2,5-bis(dipropylaminomethyl)furan based on the methyl ester of pyromucic acid.

We have shown in our work that the reaction of 2,5-bis(chloromethyl)furan with secondary amines (aliphatic, aliphatic-aromatic, heterocyclic) gives the corresponding N-substituted 2,5-bis(aminomethyl)furans in sufficiently good yields. Thus, in the action on 2,5-bis(chloromethyl)furan (I) of dimethyl- and diethylamine, N-ethyl-aniline, pyrrolidine, piperidine, and morpholine, we obtained the corresponding 2,5-bis(dimethylaminomethyl)furan (75.5%) [3], 2,5-bis(diethylaminomethyl)furan (61%) [3], 2,5-bis(N-ethyl-N-phenylaminomethyl)furan (40%), 2,5-bis(N-pyrrolidinomethyl)furan (62%), 2,5-bis(piperidinomethyl)furan (70.5%) [3], and 2,5-bis(N-morpholinomethyl)furan (62%) [3].



To obtain the diprimary diamines of the furan series we reacted 2,5-bis(chloromethyl)furan with potassium phthalimide and by the action of hydrazine hydrate [4] on the resulting diphtalide we obtained 2,5-bis(aminomethyl)furan with a yield of 40%.



EXPERIMENTAL

2,5-bis(N-ethyl-N-phenylaminomethyl)furan. We added 8.5 g of 2,5-bis(chloromethyl)furan in ether dropwise to a mixture of 19.5 g of freshly distilled ethylaniline and 9.1 g of powdered potassium hydroxide. After heating for a half hour at 40-45° and 12 hours standing, the mixture was treated with 50 ml of water, the ether layer was separated and the water was extracted with ether. The ether extract was dried with sodium hydroxide. After distillation of the ether the solid residue was treated with alcohol. We obtained 6.0 g (40%) of colorless crystals; m. p. 49-50°.

Found %: C 79.10, 79.12; H 6.03, 7.80; N 8.26, 8.51. $C_{22}H_{26}ON_2$. Calculated %: C 79.00; H 7.84; N 8.38.

It did not form a crystalline dipicrate or dimethiodide.

2,5-Bis(N-pyrrolidinomethyl)furan. To a mixture of 10.1 g of pyrrolidine and 8.5 g of powdered potassium hydroxide with periodic cooling with ice water we added dropwise over 20 minutes 8.25 g of (I) in 10 ml of absolute ether. After 12 hours water was added to solution of the precipitate and the water layer was extracted with ether. The ether extract was dried with potassium hydroxide; after distillation of the ether, the residue was distilled in a vacuum. We obtained 7 g (62%).

B. p. 163-164° (10 mm), n_D^{20} 1.5116, d_4^{20} 1.0163, MR_D 68.75. $C_{14}H_{22}ON_2F_2$. Calculated 68.84.

Found %: C 72.20, 72.02; H 9.51, 9.52; N 11.92, 11.91. $C_{14}H_{22}ON_2$. Calculated %: C 71.79; H 9.40; N 11.96.

The dimethiodide was obtained by adding methyl iodide to an alcoholic solution of the amine; m. p. 152-154° (from anhydrous alcohol).

Found %: C 37.05, 37.14; H 5.72, 5.66. $C_{16}H_{28}ON_2I_2$. Calculated %: C 37.06; H 5.40.

The dipicrate precipitated when saturated alcoholic solutions of the reagents were mixed; m. p. 173-174° (from alcohol).

Found %: C 45.08, 45.27; H 4.02, 4.02. $C_{26}H_{28}O_{15}N_8$. Calculated %: C 45.09; H 4.04.

2,5-Bis(phthalimidomethyl)furan. A mixture of 9.9 g of 2,5-bis(chloromethyl)-furan and 22.2 g of potassium phthalimide in 100 ml of freshly distilled dimethylformamide was boiled for three hours in a flask with a reflux condenser. The crystals which precipitated on cooling were filtered off, washed with dimethylformamide, and treated with 200 ml of cold water. We obtained 18 g (76%); m. p. 282-283°, colorless crystals which sublimed in a vacuum.

Found %: C 68.42, 68.53; H 3.81, 3.69. $C_{22}H_{14}O_5N_2$. Calculated %: C 68.39; H 3.62.

2,5-Bis(aminomethyl)furan. A mixture of 32 g of diphthalide and 9.6 g of 85% hydrazine hydrate in 200 ml of alcohol was boiled for two hours. After cooling, the precipitate was crushed and the mixture was boiled for one hour more; then it was cooled and to it was added 50 ml of concentrated hydrochloric acid. The precipitate of phthalyl hydrazine was filtered off and washed with alcohol. The alcohol solution was evaporated in a vacuum to dryness, and the residue, 2,5-bis(aminomethyl)furan dihydrochloride, was treated with 30 g of sodium hydroxide and 30 ml of 40% sodium hydroxide. The brown, oily layer which separated was extracted three times with diethylamine (40 ml). After drying with sodium hydroxide and distilling off the diethylamine in a vacuum, the residue was distilled in a stream of nitrogen. We obtained 4.2 g (40%) of a colorless liquid which fumed in air.

B. p. 105-106° (6 mm), 87-88° (2 mm), n_D^{20} 1.5280, d_4^{20} 1.1363, MR_D 34.14. $C_6H_{10}ON_2F_2$. Calculated: 35.26.

Found %: C 56.74, 56.68; H 8.21, 8.18; N 22.20, 22.03. $C_6H_{10}ON_2$. Calculated %: C 57.12; H 7.99; N 22.21.

The dipicrate did not melt sharply and decomposed above 200°.

Found %: C 37.26, 37.43; H 2.98, 2.96. $C_{18}H_{16}O_{15}N_8$. Calculated %: C 37.0; H 2.76.

2,5-Bis(N-phenylureidomethyl)furan, obtained by the action of phenyl isocyanate on 2,5-bis(aminomethyl)-furan, was washed with ligroin; m. p. 234-235° (from anhydrous alcohol).

Found %: C 65.67, 65.59; H 5.58, 5.62. $C_{20}H_{20}OCN_4$. Calculated %: C 65.92; H 5.53.

2,5-Bis(benzoylaminomethyl)furan was obtained by mixing an ether solution of benzoyl chloride and an ether solution of 2,5-bis(aminomethyl)furan in the presence of potash; m. p. 139° (from anhydrous benzene).

Found %: C 72.12, 72.20; H 5.76, 5.49. $C_{20}H_{18}O_3N_2$. Calculated %: C 71.84; H 5.43.

SUMMARY

The reaction of 2,5-bis(chloromethyl)furan with secondary aliphatic, aliphatic-aromatic, and heterocyclic amines is a general method for obtaining the difficultly available symmetrical tertiary diamines of the furan series; the reaction with potassium phthalimide permits preparation of a related substance among the diamines of this type, the primary diamine, 2,5-bis(aminomethyl)furan.

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* Original Russian pagination. See C. B. translation.

THE SYNTHESIS OF SOME MERCURY ORGANIC SALTS OF THE TYPE $p\text{-XC}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOR}$

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Previously we studied the kinetics of the reaction of electrophilic substituents on saturated carbon atoms in the case of the symmetrization reaction of ethyl and *l* menthyl esters of α -bromomercuriphenylacetic acid [1, 2].

To study the effect of polar and spacial factors on the rate of this reaction, we chose as model substances mercury organic salts of the general formula

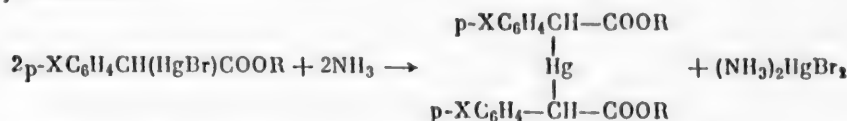


where: $X=\text{H}$, $R=\text{CH}_3$; $X=\text{H}$, $R=(\text{CH}_3)_2\text{CH}$; $X=\text{H}$, $R=(\text{CH}_3)_3\text{C}$; $X=\text{H}$, $R=\text{C}_3\text{H}_7$; $X=\text{Br}$, $R=\text{C}_2\text{H}_5$; $X=\text{Cl}$, $R=\text{C}_2\text{H}_5$; $X=\text{CH}_3$, $R=\text{C}_2\text{H}_5$.

All the mercury organic salts were first obtained by the previously studied reaction of metallic mercury and the corresponding bromoderivative [3].



Methyl bromomercuriphenylacetate and ethyl *p*-bromo- α -bromomercuriphenylacetate were symmetrized by ammonia in dry chloroform.



The starting bromoderivatives, the esters of α -bromoarylacetic acids, were first obtained from the corresponding arylacetic acids by the Hell-Volhard-Zelinskii reaction [4-14] with later treatment of the resulting acid bromide by alcohols.



EXPERIMENTAL

Isopropyl α -bromophenylacetate. To a dilute mixture of 56 g (0.46 mole) of phenylacetic acid and 3.6 g (0.116 mole) of red phosphorus was added with stirring 42 g (0.26 mole) of bromine and the mixture was heated 1.5 hours on a water bath, after which another 69 g (0.43 mole) of bromine was added. The mixture was heated until evolution of bromine vapors stopped, and then 50 g (0.84 mole) of isopropyl alcohol was added to it and the mixture was heated for four hours. The product was extracted with ether, washed with water, dilute soda solution, and with water again, dried over sodium sulfate, and vacuum distilled. Yield 64%. B. p. 125-130° (15 mm).

Nonyl α -bromophenylacetate was obtained from 36 g (0.13 mole) of α -bromophenylacetyl bromide and 37 g (0.25 mole) of nonyl alcohol. Treatment and isolation of the resulting product were carried out by the method described above. Yield 74%. B. p. 185-190° (9 mm).

Tert-butyl α -bromophenylacetate was obtained by an analogous method. Yield 72%. B. p. 143-145° (6 mm).

Ethyl p-bromo- α -bromophenylacetate. To a mixture of 35.7 g (0.17 mole) of p-bromophenylacetic acid [15-17] and 1.26 g (0.041 mole) of red phosphorus in dry chloroform with stirring was added 8.5 ml (0.16 mole) of bromine. The mixture was heated for 1.5 hours on a water bath, after which 8.8 g (0.17 mole) more bromine was added. The mixture was heated until evolution of bromine vapor stopped, 19.4 ml (0.34 mole) of anhydrous alcohol was added, and the mixture was heated for four hours more. The product was extracted with ether washed with water, with dilute soda solution, and with water, dried over sodium sulfate, and vacuum distilled. Yield 75%.

B. p. 134-136° (8 mm), d_4^{20} 1.6255, n_D^{20} 1.5349, MR_D 61.65; calc. 61.96.

Found %: C 37.49, 37.72; H 3.10, 3.19. $C_{10}H_{10}O_2Br_2$. Calculated %: C 37.27; H 3.13.

In an analogous way we obtained the two following substances.

Ethyl α -bromo-p-tolylacetate from p-tolylacetic acid [18-20] with a yield of 76%.

B. p. 126-128° (1.5 mm), d_4^{20} 1.3530, n_D^{20} 1.5353, MR_D 59.17; calc. 58.82.

Found %: C 51.85, 51.99; H 5.11, 5.06. $C_{11}H_{13}O_2Br$. Calculated %: C 51.38; H 5.09.

Ethyl p-chloro- α -bromophenylacetate from p-chlorophenylacetic acid [21] with a yield of 70%.

B. p. 147-148° (5 mm), n_D^{20} 1.5503, d_4^{20} 1.5400, MR_D 57.24; calc. 57.07.

Found %: C 43.65, 43.85; H 3.84, 3.76. $C_{10}H_{10}O_2ClBr$. Calculated %: C 43.25; H 3.62.

Methyl α -bromomercuriphenylacetate. Eighteen g (0.08 mole) of methyl α -bromophenylacetate was shaken for two hours with 81 g (0.4 mole) of metallic mercury. The product was extracted with hot acetone. Yield 80%. M. p. 92.5-94° (from alcohol).

Found %: C 25.72, 25.73; H 2.35, 2.30. $C_9H_9O_2BrHg$. Calculated %: C 25.23; H 2.16.

In an analogous way were obtained the following five substances.

Isopropyl α -bromomercuriphenylacetate with a yield of 68%. M. p. 84-85° (from alcohol).

Found %: C 28.78, 28.78; H 2.97, 3.08. $C_{11}H_{13}O_2BrHg$. Calculated %: C 28.86; H 2.86.

Tert-butyl α -bromomercuriphenylacetate with a yield of 43%. M. p. 141-142° (from alcohol).

Found %: C 30.47, 30.45; H 3.19, 3.10. $C_{12}H_{15}O_2BrHg$. Calculated %: C 30.50; H 3.20.

Nonyl α -bromomercuriphenylacetate with yield of 33%. Yellow oil.

Found %: C 37.99, 37.59; H 4.35, 4.28. $C_{17}H_{25}O_2BrHg$. Calculated %: C 37.68; H 4.66.

Ethyl p-chloro- α -bromomercuriphenylacetate with yield of 49%. M. p. 120-120.5° (from alcohol).

Found %: C 22.93, 23.09; H 2.04, 2.17. $C_{10}H_{10}O_2Br_2Hg$. Calculated %: C 22.98; H 1.93.

Ethyl p-chloro- α -bromomercuriphenylacetate with yield of 34%. M. p. 111-111.5° (from alcohol).

Found %: C 25.47, 25.48; H 2.28, 2.36. $C_{10}H_{10}O_2ClBrHg$. Calculated %: C 25.11; H 2.11.

Ethyl α -bromomercuri-p-tolylacetate was obtained by shaking ethyl α -bromo-p-tolylacetate with metallic mercury in the presence of benzoyl peroxide (a small amount of the ester was first heated with the peroxide) with a yield of 15%. M. p. 144.5-145° (from alcohol).

Found %: C 29.19, 28.99; H 3.08, 2.95. $C_{11}H_{13}O_2BrHg$. Calculated %: C 28.86; H 2.86.

α -Mercury-bis(methyl phenylacetate). In a solution of 5 g (0.01 mole) of methyl α -bromomercuriphenylacetate in dry chloroform in the cold was passed a stream of dry ammonia for 10 minutes. The precipitate of $(\text{NH}_3)_2\text{HgBr}_2$ which formed was filtered off, the filtrate was evaporated in the dark; the oil which remained after evaporation of the chloroform gradually crystallized. The crystals were washed with cold ligroin and methyl alcohol. Yield 74%. M. p. 140-141° (from alcohol).

Found %: Hg 40.56, 40.42. $\text{C}_{18}\text{H}_{18}\text{O}_4\text{Hg}$. Calculated %: Hg 40.21.

In an analogous way was prepared α -mercury-bis(ethyl *p*-bromophenylacetate) with a yield of 80%. M. p. 124-125° (from alcohol).

Found %: C 35.34, 35.45; H 2.86, 2.87. $\text{C}_{20}\text{H}_{22}\text{O}_4\text{BHg}$. Calculated %: C 35.08; H 2.95.

SUMMARY

1. We have synthesized for the first time the mercury organic salts of the type $p\text{-XC}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOR}$, where: $\text{X}=\text{H}$, $\text{R}=\text{CH}_3$; $\text{X}=\text{H}$, $\text{R}=(\text{CH}_3)_2\text{CH}$; $\text{X}=\text{H}$, $\text{R}=(\text{CH}_3)_3\text{C}$; $\text{X}=\text{H}$, $\text{R}=\text{C}_6\text{H}_5$; $\text{X}=\text{Br}$, $\text{R}=\text{C}_2\text{H}_5$; $\text{X}=\text{Cl}$, $\text{R}=\text{C}_2\text{H}_5$; $\text{X}=\text{CH}_3$, $\text{R}=\text{C}_2\text{H}_5$.

2. The symmetrization of methyl α -bromomercuriphenylacetate and ethyl α -bromomercuri-*p*-bromophenylacetate by ammonia in chloroform has given for the first time α -mercury-bis(methyl phenylacetate) and α -mercury-bis(ethyl *p*-bromophenylacetate).

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THE AUTOOXIDATION OF *p*-sec-BUTYLTOLUENE

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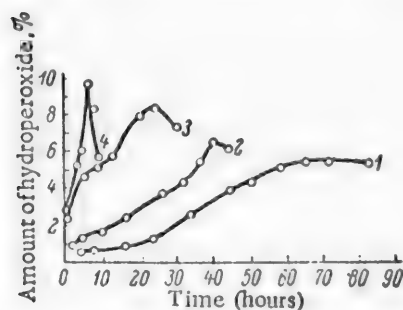
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In the liquid phase oxidation of dialkylbenzenes there are a fairly large number of reports, chiefly in the patent literature; the main attention has been directed to the autooxidation of *p*-cymene [1]. The oxidation of aromatic hydrocarbons with two different alkyl radicals has been especially poorly studied.

The oxidation of *p*-sec-butyltoluene has been considered in a work [2] where the authors on the basis of an analysis of the products of splitting with hydroperoxide showed that both radicals are oxidized; however, in this paper quantitative data on the degree of oxidation of both alkyl groups are lacking.



Rate of oxidation of *p*-sec-butyltoluene at 110°. In the presence of 1) manganese resinate; 2) manganese resinate and calcium hydroxide; 3) manganese resinate, sodium hydroxide, and isopropylbenzene hydroperoxide; 4) manganese resinate and isopropylbenzene hydroperoxide.

The present work studies the autooxidation of *p*-sec-butyltoluene with quantitative determination of the products of acid splitting by hydroperoxide and also of the products obtained in the oxidation of *p*-sec-butyltoluene to complete disappearance of the hydroperoxide from the reaction mass. The oxidation was studied at various temperatures and it was shown that the most favorable was 110°. As initiator of oxidation we used manganese resinate with additions: calcium hydroxide, sodium hydroxide, cobalt acetate, sodium stearate, which, as had been shown before [3], have a favorable effect on the depth of autooxidation; we also used 86% isopropylbenzene hydroperoxide. As the figure shows, the most energetic oxidation occurs in the presence of manganese resinate and isopropylbenzene hydroperoxide (after six hours the maximum concentration of hydroperoxide was 9.5%). In the presence of alkali, the hydroperoxide initiates oxidation much more slowly. The addition to the manganese resinate of cobalt acetate and sodium stearate raises the total yield of products of oxidation, but the maximum concentration of hydroperoxide in this case does not exceed 1%.

In the oxidation of *p*-sec-butyltoluene in the presence of manganese resinate and calcium hydroxide (rate of passing air 18 liters/hour and a time of 33 hours) after treatment of the reaction mass with concentrated hydrochloric acid, we isolated *p*-methylacetophenone, *p*-cresol, *p*-tolylmethylethyl carbinol, *p*-acetylbenzoic acid, *p*-sec-butylbenzoic acid, and *p*-sec-butylbenzyl alcohol in molar ratios of 22.2 : 5.8 : 8 : 2.6 : 18 : 1.

In the oxidation of *p*-sec-butyltoluene in the presence of manganese resinate, sodium stearate, cobalt acetate, sodium hydroxide, and calcium hydroxide the rate of passing air was 18 liters/hour, time 89 hours, and *p*-methylacetophenone, *p*-tolylmethylethyl carbinol, *p*-acetylbenzoic acid, and *p*-sec-butylbenzyl alcohol were isolated in molar ratios of 37.5 : 15 : 6 : 40.5 : 1, respectively.

Thus, in *p*-sec-butyltoluene oxidation occurs on the primary carbon atom of the methyl radical with formation of *p*-sec-butylbenzyl hydroperoxide, and also on the tertiary α -atom of carbon of the secondary butyl

radical with formation of α -methyl- α -ethyl-p-methylbenzyl hydroperoxide. Here oxidation of the secondary butyl radical in the presence of manganese resinate and alkaline additions occurs 1.8 times faster than of the methyl radical, and in the presence of magnesium resinate, sodium stearate, cobalt acetate, and alkaline additions, 1.2 times faster, without considering the p-acetylbenzoic acid, which can result from oxidation of p-methylacetophenone [4] and from n-sec-butylbenzoic acid).

EXPERIMENTAL

p-sec-Butyltoluene was obtained by alkylation of toluene with pseudobutylene in the presence of a $\text{BF}_3 \cdot \text{H}_3\text{PO}_4$ catalyst in the molar ratio 2.6 : 1 : 0.37 at 30° with an average yield of 90% [5]. The alkylation product was treated repeatedly with concentrated sulfuric acid, washed with 10% sodium hydroxide, then with water, dried over sodium hydroxide and distilled over sodium: b. p. 192-193°, n_D^{20} 1.4930, d_4^{20} 0.8664.

Autooxidation of p-sec-butyltoluene. In a glass column reactor placed in an oil thermostat was put p-sec-butyltoluene (1), the initiator, and the alkaline additive. The mixture was heated to 110° and air was passed through at a rate of 18 liters/hour either to formation of maximum concentration of hydroperoxide, or to its complete disappearance from the reaction mixture. The content of hydroperoxide was determined each 2-6 hours iodometrically. The results of the experiments are given in Table 1.

TABLE 1

Taken for oxidation per 1 mole p-sec-butyl-toluene			Maximum concentration of hydroperoxide, %	Time of formation of maximum concentration of hydroperoxide, hours
Manganese resinate (in mg)	Additive			
	Name	Amount		
5			5.3	66
5	Calcium hydroxide	1.2 g	4.2	36
5	Isopropylbenzene hydroperoxide	2 ml	9.5	6
5	Isopropylbenzene hydroperoxide	2 ml	9.4	26
	Calcium hydroxide	1.2 g		
10	Calcium hydroxide	1.2 g	6.5	40
3	Sodium hydroxide	1.0 g	2.2	26
3	Sodium hydroxide	1.0 g	8.3	24
	Isopropylbenzene hydroperoxide	2 ml		

Acid splitting of p-sec-butyltoluene hydroperoxide. To 142.2 g of reaction mixture containing 4.7% hydroperoxide was added dropwise 20 ml of concentrated hydrochloric acid during 16 hours at room temperature. The acid product was extracted with 10% alkali. After corresponding treatment and distillation we isolated from the neutral layer 95.4 g of unoxidized hydrocarbon; 18.1 g of a mixture which contained 8.2% p-methylacetophenone, 2.8% p-tolylmethylethyl carbinol, 0.4% p-sec-butylbenzyl alcohol, and 3.0 g of tar; from the alkali layer, 2.3 g (2.2%) of p-cresol, 1.6 g (0.9%) of p-tolylmethylethyl carbinol, and 2.5 g (7.1%) of p-sec-butylbenzoic acid.

Oxidation of p-sec-butyltoluene to disappearance of hydroperoxide from the reaction mass was carried out as described above with only this difference, that after reaching the maximum concentration of hydroperoxide air was further passed in. The results of the experiments are given in Table 2.

Oxidation of p-sec-butylbenzoic acid. We oxidized 19.2 g of p-sec-butylbenzoic acid, obtained by autooxidation of p-sec-butyltoluene (b. p. 127-130° at 2 mm, not recrystallized) for 82 hours in the presence of 0.3 mg of manganese resinate, 17 mg of cobalt acetate, and 60 mg of sodium stearate at 110°. The crystals of p-acetylbenzoic acid which precipitated were filtered off from the oil and washed with methanol. Yield 5.4 g (30.5%).

TABLE 2

Catalyst used (in mg) per 1 mole hydrocarbon	Time of oxidation, hours	Maximum amount of peroxide, %	Yield of oxidation products, %					
			p-methyl-acetophenone	p-cresol	p-tolyl-methyl-ethyl carbinol	p-acetyl-benzoic acid	p-sec-butyl-benzoic acid	p-sec-butyl-benzyl alcohol
Manganese resinate, 1; sodium hydroxide, 100; cobalt acetate, 70	69	2.9	5.9	0.7	2.3	-	4.8	0.13
Manganese resinate, 1; cobalt acetate, 150; sodium stearate, 500; sodium hydroxide, 100; calcium hydroxide 300	46	0.6	9.2	-	5.2	4.3	13.5	0.3
Manganese resinate, 1; cobalt acetate, 150; sodium stearate, 500; sodium hydroxide, 100; calcium hydroxide, 300	89	1	13.6	-	7.8	2.2	14.7	0.4

Characteristics of the oxidation products. *p*-Cresol was characterized through *p*-methylphenoxyacetic acid with m. p. 136.4° which corresponded to the literature [6].

p-sec-Butylbenzoic acid, a viscous yellow mass with b. p. 130-140° (2 mm), n_D^{20} 1.5210, d_4^{20} 1.0740, crystallized on standing in the form of white needles with m. p. 91.5-92° (from alcohol-water mixture); the literature gives [7]: m. p. 90-92.5°. A mixed m. p. with *p*-sec-butylbenzoic acid obtained by synthesis [7] gave no depression.

p-Acetylbenzoic acid, a finely crystalline powder with m. p. 203-204° (sublimed and recrystallized from alcohol); its methyl ester had m. p. 89.5-90°; the literature [8] gives: for the acid, m. p. 203°; for the ester, m. p. 92°.

p-Methylacetophenone was extracted from a mixture which contained 78% of the ketone and 22% primary and tertiary alcohols as its 2,4-dinitrophenylhydrazone with m. p. 246-7° (from acetic acid); the literature [6] gives m. p. 248°. It was determined quantitatively by oximation [9].

p-sec-Butylbenzyl alcohol was determined by quantitative acetylation with a 12% solution of acetic anhydride in pyridine [10].

p-Tolylmethyl ethyl carbinol was determined quantitatively by dehydration over potassium bisulfate in a medium of diisopropylbenzene followed by titration of the water formed with the Fischer reagent [11].

SUMMARY

We have studied the autooxidation of *p*-sec-butyltoluene by oxygen of the air in the presence of manganese resinate, sodium hydroxide, and other additives at 110°. We have shown that oxidation on the sec-butyl radical occurs 1.8 times more easily than in the primary methyl group under mild conditions, and 1.2 times more easily under severe conditions.

The chief oxidation products are *p*-methylacetophenone, *p*-tolylmethyl ethyl carbinol, and *p*-sec-butylbenzoic acid. We have found that *p*-sec-butylbenzoic acid can be oxidized by oxygen of the air to give *p*-acetylbenzoic acid with a yield of 30.5%.

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ESTERS OF CYCLOPENTADIENYL-, 1-INDENYL-, AND -FLUORENYLPHOSPHONOUS ACIDS

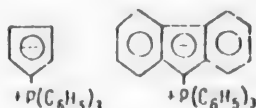
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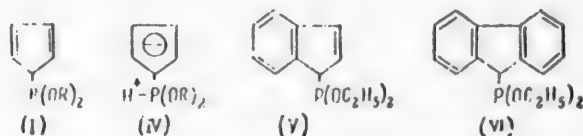
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A specific property of cyclopentadiene and its derivatives is the ability to form a cyclopentadienyl anion with a definite aromatic character. This determines the acid properties of derivatives of cyclopentadiene, indene, and fluorene and the stability of "ylides", in which the anion of the corresponding hydrocarbon is combined with an onium heteroatom. It is known, for example, that the bipolar structures of phosphinemethylenes (phosphorus ylides) are in general very unstable [1] but show great stability in those cases when the anion centers are cyclopentadiene [2] and fluorene [3] nuclei.

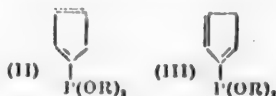


In connection with the problem of tautomerism of compounds of trivalent phosphorus, it was of interest to synthesize esters of cyclopentadienylphosphonous acid in order to study their properties and establish their structures. There are two ascribed to these substances, covalent, with a trivalent atom of phosphorus (I)* and an "ylide" with an aromatic cyclopentadienyl residue (IV). The origin of this structure from the covalent form can be considered the result of a transfer of a proton from the cyclopentadienyl ring to an atom of trivalent phosphorus.



The known acid properties of the methylene group of cyclopentadiene and its derivatives and the basic properties of compounds of trivalent phosphorus (ability of unshared pairs of electrons of phosphorus to combine with protons) can determine such transfer. The possibility is also not excluded of a tautomeric relationship $(I) \rightleftharpoons$

* Besides structure (I) other structures (II) and (III) are possible for the covalent form, reciprocally related through



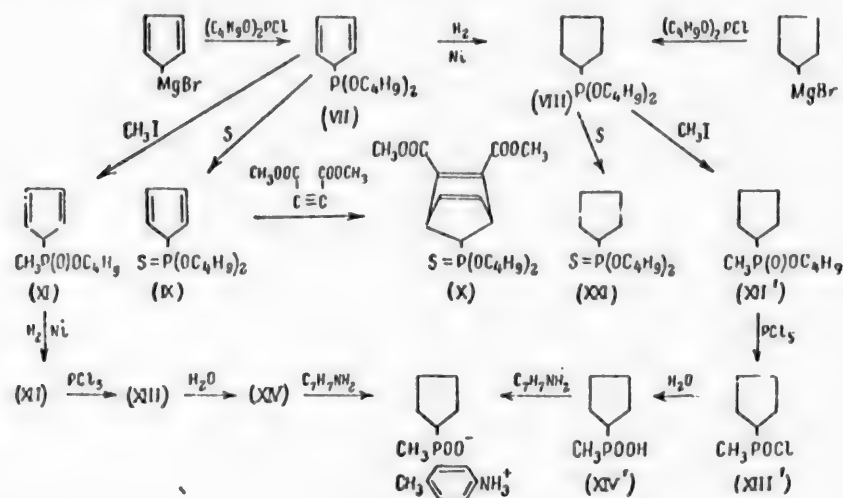
a three carbon prototropic intermediate. This question is not considered in the present paper.

(IV). In order to test the possibility of occurrence of a structure of the "ylide" type it was also interesting to include in the investigation the corresponding indene (V) and fluorene (VI) derivatives.

The synthesis of all these compounds was carried out by the method which we worked out previously [4, 5] based on replacement of chlorine atoms of dialkylchlorophosphite by different radicals in the reaction with magnesium and lithium organic derivatives at low temperatures.

The dibutyl ester of cyclopentadienylphosphonous acid (VII) was obtained with a yield of 33.4% by the reaction of cyclopentadienylmagnesium bromide with dibutylchlorophosphite at -60° . Sodium cyclopentadienyl gave a higher yield, but its use is connected with difficulties in separating the sodium chloride which is formed.

The first results of the study of these compounds has already revealed an advantage for the covalent structure (I) [or (II) or (III)] and are against the "ylide" structure (IV).



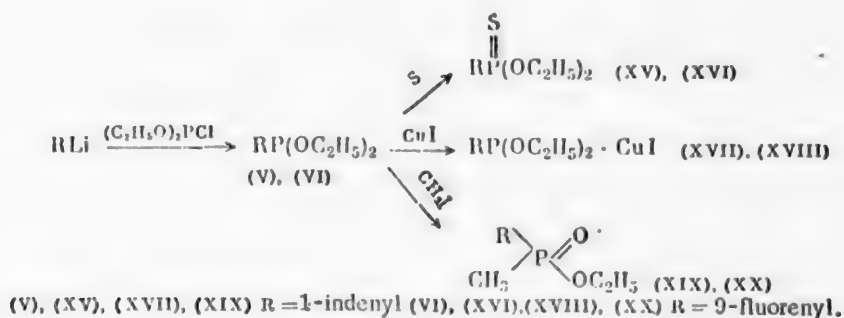
Freshly distilled dibutyl ester of cyclopentadienylphosphonous acid (VII) is a colorless liquid which almost immediately darkens in the air. In hydrogenation in the presence of a skeletal nickel catalyst at room temperature, it absorbs two moles of hydrogen and is converted to the dibutyl ester of cyclopentylphosphonous acid (VIII) whose structure was confirmed by comparison with the ester obtained earlier [6] from dibutylchlorophosphite and cyclopentylmagnesium bromide. The easy hydrogenation of the ester of cyclopentadienylphosphonous acid (VII) speaks in favor of the diene structure, since in the case of the "ylide" form (IV) the aromatic system of the cyclopentadiene anion would be more resistant to hydrogenation.

The dibutyl ester of cyclopentadienylphosphonous acid (VII) adds sulfur energetically with formation of the ester of cyclopentadienylthiophosphonic acid (IX) which with dimethyl acetylenedicarboxylate gives the corresponding adduct (X) which shows the presence of the diene system in the thiophosphonic derivative (IX). As a result of the Arbuzov rearrangement the dibutyl ester of cyclopentadienylphosphonous acid (VII) gave a secondary methylcyclopentadienylphosphinic ester (XI) which was hydrogenated to the corresponding cyclopentyl derivative (XII), and converted further through the acid chloride (XIII) to the acid (XIV) whose *p*-toluidine salt was identical with the *p*-toluidine salt of methylcyclopentylphosphinic acid (XIV') obtained from the dibutyl ester of cyclopentylphosphonous acid (VIII) by analogous reactions. These transformations show the structure of the dibutyl ester of cyclopentadienylphosphonous acid (VII) as a derivative of trivalent phosphorus (covalent structure). This conclusion is also confirmed by the combination light scattering spectrum* in which there are intense bands at 1492 cm^{-1} , characteristic for the diene system of cyclopentadiene [7], and absorption is absent in the region $2350\text{--}2440\text{ cm}^{-1}$ which corresponds to valence oscillation of the P-H bond [8].

* Besides formula (X), derived from structure (I) we can also consider the isomeric formulas corresponding to structures (II) and (III).

** The combination scattering spectrum of the dibutyl ester of cyclopentadienylphosphonous acid was photographed and interpreted by M. E. Movsesyan, to whom the authors express thanks.

The esters of 1-indenyl- and 9-fluorenylphosphonous acids (V) and (VI) whose synthesis from the corresponding lithium organic compounds and diethylchlorophosphite was described earlier by us [5] also have the properties of derivatives of trivalent phosphorus. They easily add sulfur and cuprous iodide with formation of the corresponding thiophosphonic esters (XV) and (XVI), and the complex compounds with cuprous iodide (XVII) and (XVIII), and also undergo the Arbusov rearrangement with methyl iodide, as a result of which they give esters of secondary phosphinic acids (XIX) and (XX).



Thus the transformations which we studied indicate that these phosphonous esters are derivatives of trivalent phosphorus with covalent and not "ylide" structures. There remains the possibility of a tautomeric equilibrium which shifts to the side of the covalent form. However, there is still no experimental basis for a conclusion as to tautomerism*.

EXPERIMENTAL

All the operations were carried out in an atmosphere of dry, purified nitrogen; the solvents and reagents were carefully dried.

Dibutyl ester of cyclopentadienylphosphonous acid (VII). a) We added 22 g (0.334 mole) of freshly distilled cyclopentadiene in 25 ml of toluene with stirring and weak boiling to a solution of ethylmagnesium bromide (from 6.5 g of magnesium and 29 g of ethyl bromide) in 80 ml of ether and 80 ml of toluene. The solution was boiled for two hours, cooled (sometimes a precipitate appeared) and added to 53 g (0.25 mole) of dibutylchlorophosphite in 50 ml of ether with energetic stirring and a temperature of the reaction mixture of $-60 \pm 5^\circ$. The solvent was removed in a vacuum, the residue was treated with 200 ml of ligroin, the mixture was stirred, filtered, and the precipitate was washed with ligroin which was added to the filtrate. The solvent was removed in a vacuum and the residue was distilled. After two distillations we obtained 20.2 g (33.4%) of substance: b. p. $80-81^\circ$ (1 mm) (with slow distillation)*, n_D^{20} 1.4822, d_4^{20} 0.9610***, M_R 71.91; calc. 71.23; ΔM_R 0.68.

Found %: C 64.4, 64.5; H 9.6, 9.7; P 12.9, 12.6. $\text{C}_{13}\text{H}_{23}\text{O}_2\text{P}$. Calculated %: C 64.4; H 9.6; P 12.8.

*The constants of the dibutyl ester of cyclopentadienylphosphonous acid change on standing, and again are restored by vacuum distillation. The substance which has stood adds sulfur and undergoes the Arbusov rearrangement as easily as after fresh distillation. This excludes the explanation of the process as a reversible transformation of the covalent form of ester into the "ylide". The reason for the change in constants requires special study. It is possible that there occurs here a reversible dimerization of the diene, although the possibility is not excluded of a tautomeric transformation $(\text{I}) \rightleftharpoons (\text{II}) \rightleftharpoons (\text{III})$. The esters of cyclopentadienylthiophosphonic and secondary methylcyclopentadienylphosphinic acids (IX) and (XI) also show a change in constants on standing and regain these when distilled in a vacuum.

**At first at about the same temperature there distilled over an unidentified substance and its mixture with the dibutyl ester of cyclopentadienylphosphonous acid; then with stronger heating of the bath ($150-200^\circ$) the dibutyl ester of cyclopentadienylphosphonous acid slowly distilled. The first fraction was separated, using as a guide the change in index of refraction and specific gravity.

***The constants changed on standing, and after 3-4 weeks reached constant values: n_D^{20} 1.4950, d_4^{20} 1.0110.

Combination scattering spectrum (in cm^{-1}) (intensity described visually on the ten point system): 450 (0), 517 (0), 556 (0), 673 (0), 696 (1 b), 713 (1), 770 (0), 798 (0), 817 (0), 835 (1), 907 (0), 930 (0), 948 (1), 992 (3), 1023 (1 b), 1070 (1 b), 1102 (3), 1122 (2), 1136 (0), 1152 (0), 1190 (0), 1215 (1), 1250 (0), 1296 (2), 1321 (0), 1348 (3), 1372 (3 b), 1427 (1), 1452 (1), 1479 (1), 1492 (10), 1545 (0), 1575 (1), 1603 (0), 2873 (10), 2909 (10), 2939 (6), 2965 (3), 3085 (5 b).

b) A solution of sodium cyclopentadiene in tetrahydrofuran [9] (2.5 g of sodium, 8 g of freshly distilled cyclopentadiene, 40 ml of tetrahydrofuran) was added with stirring to 21.6 g (0.10 mole) of dibutylchlorophosphite in 50 ml of ether at -60° . The solvent was removed in a vacuum and the precipitate was treated with 100 ml of ligroin and 4-5 g of anhydrous ammonium chloride; the mixture remained overnight for coagulation of the sodium chloride. The precipitate was filtered off and washed with ligroin; the filtrate was concentrated and distilled in a vacuum. The yield of dibutyl ester of cyclopentadienylphosphonous acid was 55%, n_D^{20} 1.4820.

Hydrogenation of the dibutyl ester of cyclopentadienylphosphonous acid (VII). We shook 8.3 g of the dibutyl ester of cyclopentadienylphosphonous acid (VII) in 20 ml of dioxane in an atmosphere of hydrogen and in the presence of a skeletal nickel catalyst at room temperature and atmospheric pressure. After absorption of 82.5% of the theoretical amount of hydrogen (14 hours) hydrogenation practically stopped. The catalyst was filtered off, the dioxane was removed in a vacuum, and the residue was distilled. We obtained 6.3 g (74.7%) of the substance; b. p. $83-83.5^\circ$ (1.5 mm), n_D^{20} 1.4620, d_4^{20} 0.9314, MR_D 72.68; calc. 72.16.

Found %: C 63.2, 63.3; H 11.2, 11.2; P 12.6, 12.7. $C_{13}H_{27}O_2P$. Calculated %: C 63.4; H 11.1; P 12.6.

The literature gives for the dibutyl ester of cyclopentylphosphonous acid (VIII) [6]; b. p. $77-78^\circ$ (1 mm), n_D^{20} 1.4595, d_4^{20} 0.9284, MR_D 72.57.

Addition of sulfur to the dibutyl ester of cyclopentadienylphosphonous acid (VII). We added 1.4 g (0.04 g-atom) of sulfur with stirring to 10.3 g (0.04 mole) of freshly distilled dibutyl ester of cyclopentadienylphosphonous acid in 50 ml of ether at 0° . After solution of the sulfur, the ether was removed and the residue was distilled in a vacuum. The yield of dibutyl ester of cyclopentadienylthiophosphonic acid (IX) was 9 g (77%).

B. p. (with slow distillation) $114-115^\circ$ (1 mm), n_D^{20} 1.5070, d_4^{20} 1.0475*, MR_D 77.96; calc. 77.46.

Found %: C 57.2, 57.4; H 8.5, 8.6; P 11.3, 11.0; S 11.5, 11.5. $C_{13}H_{23}O_2PS$. Calculated %: C 56.9; H 8.5; P 11.3; S 11.7.

Adduct of dimethyl acetylenedicarboxylate with the dibutyl ester of cyclopentadienylthiophosphonic acid (X). A mixture of 6.4 g (0.023 mole) of freshly distilled dibutyl ester of cyclopentadienylthiophosphonic acid (IX) and 5 g (0.035 mole) of dimethyl acetylenedicarboxylate [10] was heated for two hours at $110-120^\circ$ and fractionated. Yield of adduct (X) 7 g (72.2%); b. p. $194-195^\circ$ (2 mm), n_D^{20} 1.5056, d_4^{20} 1.1454, MR_D 107.9; calc. 106.3.

Found %: C 55.2, 55.1; H 7.1, 7.0; P 7.6, 7.5; S 7.1, 7.1. $C_{19}H_{29}O_6PS$. Calculated %: C 54.8; H 7.0; P 7.4; S 7.7.

Dibutyl ester of cyclopentylthiophosphonic acid (XXI) was obtained by adding 0.676 g (0.02 g-atom) sulfur to 5.2 g (0.02 mole) of the dibutyl ester of cyclopentylphosphonous acid (VIII) [6]. Yield 5.35 g (90.8%); b. p. $108-108.5^\circ$ (1 mm), n_D^{20} 1.4793, d_4^{20} 1.0035, MR_D 78.68; calc. 78.39.

Found %: C 55.7, 55.8; H 9.8, 9.7; P 10.9, 10.9; S 11.6, 11.8. $C_{13}H_{27}O_2PS$. Calculated %: C 56.1; H 9.7; P 11.1; S 11.5.

Arbuzov rearrangement of the dibutyl ester of cyclopentadienylphosphonous acid (VII). Twenty-five ml of methyl iodide was added with stirring to 12.3 g of freshly distilled dibutyl ester of cyclopentadienylphosphonous acid (VII). At the end of the stormy reaction (which required cooling) the solution was boiled for two hours and fractionated. The yield of butyl ester of methylcyclopentadienylphosphinic acid (XI) was 8.95 g (88%); b. p. $91-92^\circ$ (1 mm) (slow distillation), n_D^{20} 1.4918, d_4^{20} 1.0512*, MR_D 55.22; calc. 54.99.

Found %: C 60.1, 60.3; H 8.7, 8.5; P 15.1, 15.2. $C_{10}H_{17}O_2P$. Calculated %: C 60.0; H 8.6; P 15.5.

* The constants changed on standing for 3-4 weeks, reaching a constant value of: n_D^{20} 1.5150, d_4^{20} 1.0799.

** The constants changed on standing 3-4 weeks to reach a constant value of: n_D^{20} 1.5070, d_4^{20} 1.1120.

Hydrogenation of the butyl ester of methylocyclopentadienylphosphinic acid (XI). We hydrogenated 4.5 g of freshly distilled butyl ester of methylocyclopentadienylphosphinic acid (XI) in 20 ml of dioxane in the presence of skeletal nickel catalyst at room temperature and atmospheric pressure. After 12 hours 90% of the theoretical amount of hydrogen had been absorbed. The catalyst was filtered off, the dioxane was removed in a vacuum, and the residue was distilled. The yield of butyl ester of methylocyclopentylphosphinic acid (XII) was 6.7 g (73.3%); b. p. 86-87° (1 mm), n_D^{20} 1.4643, d_4^{20} 1.0025, MR_D 56.24; calc. 55.92.

Found %: C 58.8, 59.0; H 10.2, 10.4; P 14.9, 14.9. $C_{10}H_{12}O_2P$. Calculated %: C 58.8; H 10.4; P 15.2.

Butyl ester of methylocyclopentylphosphinic acid (XII'). As in the case of the butyl ester of methylocyclopentadienylphosphinic acid (XI), we obtained from 10.7 g of dibutyl ester of cyclopentylphosphonous acid (VIII) and 25 ml of methyl iodide 8.1 g (90%) of the butyl ester of methylocyclopentylphosphinic acid (XII'); b. p. 90-91° (1 mm), n_D^{20} 1.4628, d_4^{20} 1.0026, MR_D 56.03; calc. 55.92.

Found %: C 58.6, 58.5; H 10.3, 10.1; P 15.1, 15.3. $C_{10}H_{12}O_2P$. Calculated %: C 58.8; H 10.4; P 15.2.

Methylocyclopentylphosphinic acid chloride (XIII'). We gradually added 11.5 g (0.055 mole) of phosphorus pentachloride to 10.8 g (0.053 mole) of butyl ester of methylocyclopentylphosphinic acid (XII') obtained from the dibutyl ester of cyclopentylphosphonous acid (VIII). After the end of the stormy reaction the mixture was fractionated. The yield of methylocyclopentylphosphinic acid chloride (XIII') was 6.5 g (77.5%); b. p. 80-80.5° (1 mm), n_D^{20} 1.4989, d_4^{20} 1.1800, MR_D 41.45; calc. 41.04.

Found %: C 43.2, 43.6; H 7.1, 7.4; P 18.3, 18.4. $C_6H_{12}OPCl$. Calculated %: C 43.3; H 7.3; P 18.6.

Methylocyclopentylphosphinic acid (XIV'). Two g (0.014 mole) of methylocyclopentylphosphinic acid chloride (XIII') was mixed with 0.5 g (0.028 mole) of water in 20 ml of dioxane (the mixture was heated), the dioxane was removed and the residue distilled. Yield 1.7 g (96%); b. p. 171-172.5° (2 mm), n_D^{20} 1.4900, d_4^{20} 1.1390, MR_D 37.61; calc. 37.33.

Found %: C 48.9, 48.9; H 8.8, 8.8; P 20.8, 21.0. $C_6H_{10}O_2P$. Calculated %: C 48.6; H 8.8; P 20.9.

The methylocyclopentylphosphinic acid (XIV') was also obtained by saponification of the butyl ester of methylocyclopentylphosphinic acid (XII') with a solution of potassium hydroxide (boiling for four hours).

p-Toluidide salt of methylocyclopentylphosphinic acid. When we mixed ether solutions of equimolecular amounts of p-toluidine and methylocyclopentylphosphinic acid (XIV') and distilled off the ether, crystals of the methylocyclopentylphosphinic p-toluidide precipitated. Yield 87%; m. p. 70-71° (from ligroin).

Found %: C 61.2, 61.2; H 8.7, 8.7; P 12.3, 12.1; N 5.5, 5.4. $C_{13}H_{22}O_2PN$. Calculated %: C 61.2; H 8.7; P 12.1; N 5.5.

By the above described reaction we obtained from the butyl ester of methylocyclopentylphosphinic acid (XII) prepared by hydrogenation of the corresponding cyclopentadienyl ester (XI) a p-toluidide (m. p. 70-70.5°) which gave no melting point depression with the p-toluidide of methylocyclopentylphosphinic acid.

Addition of Sulfur to Esters of 1-Indenyl- and 9-Fluorenylphosphonous Acid

Diethyl ester of 1-indenylthiophosphonic acid (XV) was obtained by adding 0.56 g (0.018 g-atom) of sulfur to 4.2 g (0.018 mole) of the diethyl ester of indenylphosphonous acid (V) in ether. Yield 4.1 g (88%); b. p. 139-140° (2 mm), n_D^{20} 1.5678, d_4^{20} 1.1514.

Found %: C 58.0, 57.9; H 6.4, 6.4; P 11.3, 11.3; S 12.0, 12.0. $C_{13}H_{17}O_2PS$. Calculated %: C 58.2; H 6.4; P 11.5; S 12.0.

Diethyl ester of 9-fluorenylthiophosphonic acid (XVI) was synthesized in an analogous way from 0.56 g (0.018 g-atom) sulfur and 5.2 g (0.018 mole) of the diethyl ester of 9-fluorenylphosphonous acid (VI). Yield 4.3 g (74.1%); b. p. 166-169° (2 mm), m. p. 66-67° (from anhydrous alcohol).

Found %: C 64.0, 63.9; H 6.1, 6.2; P 9.4, 9.3; S 10.0, 10.1. $C_{17}H_{19}O_2PS$. Calculated %: C 64.1; H 6.0; P 9.7; S 10.0.

The complex compound of diethyl ester of 1-indenylphosphonous acid with cuprous iodide (XVII) was obtained by heating the ester of phosphonous acid (V) with cuprous iodide to 150°; m. p. 126-127° (from a mixture of acetone and anhydrous alcohol).

Found %: C 36.8, 36.6; H 4.2, 4.1; I 30.0, 29.7; residue 34.8, 35.0. $C_{13}H_{17}PO_2 \cdot CuI$. Calculated %: C 36.6; H 4.0; I 29.8; $\frac{1}{2} Cu_2P_2O_7$ 35.3.

The complex compound of diethyl ester of 9-fluorenylphosphonous acid with cuprous iodide (XVIII) was obtained in an analogous way; m. p. 181.5-183° (from a mixture of anhydrous alcohol and chloroform).

Found %: C 43.1, 43.0; H 4.2, 4.1; I 26.5, 26.3; residue 31.7, 31.8. $C_{17}H_{19}PO_2 \cdot CuI$. Calculated %: C 42.8; H 4.0; I 26.6; $\frac{1}{2} Cu_2P_2O_7$ 31.6.

Arbuzov Rearrangement of Esters of 1-Indenyl- and 9-Fluorenylphosphonous Acids

Ethyl ester of methyl-1-indenylphosphinic acid (XIX) was obtained by boiling 5.8 g of diethyl ester of 1-indenylphosphonous acid (V) with an excess of methyl iodide for four hours. Yield 4.4 g (80.3%); b. p. 127.5-128.5° (1.5 mm), n_D^{20} 1.5579, d_4^{20} 1.1434.

Found %: C 64.9, 64.7; H 6.8, 6.7; P 14.1, 14.0. $C_{12}H_{15}O_2P$. Calculated %: C 64.9; H 6.8; P 13.9.

The ethyl ester of methyl-9-fluorenylphosphinic acid (XX) was synthesized in an analogous way from 5 g of diethyl ester of 9-fluorenylphosphonous acid (VI). Yield 3.7 g (77.6%); b. p. 164-166° (2 mm), m. p. 97-97.5° (from ether).

Found %: C 70.6, 70.8; H 6.1, 6.3; P 11.6, 11.6. $C_{16}H_{17}O_2P$. Calculated %: C 70.6; H 6.2; P 11.4.

SUMMARY

We have studied some chemical properties of esters of cyclopentadienyl-, 1-indenyl-, and 9-fluorenylphosphonous acids; the study of the reactions indicates the presence in the molecule of these substances of a trivalent atom of phosphorus, and also of two double bonds in the ester of cyclopentadienylphosphonous acid.

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STUDIES OF RADICAL REACTIONS OF PENTAPHENYLANTIMONY

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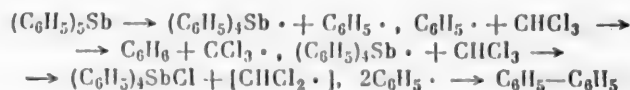
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10, pp. 3234-3237,

October, 1960

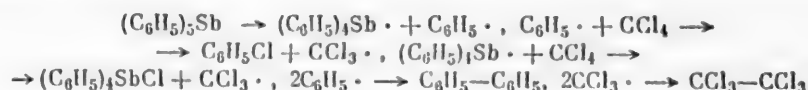
Original article submitted October 12, 1959

On the basis of results which have appeared in the literature [1], pentaphenyl derivatives of elements of Group V, subgroup nitrogen, can be divided into compounds of the type of pentaphenylphosphorus (PPP) and compounds of the type of pentaphenylantimony (PPA) since they behave differently in thermal decompositions, in reactions with halides and halogen hydrides, in complex forming reactions, and have Debye diagrams [2] which differ in intensity and structure; therefore it seemed interesting to us to continue the work begun in the study of PPP in the case of PPA. For this purpose we used the known method of investigation which had been adopted in study of the radical reactions of PPP [1, 3, 4].

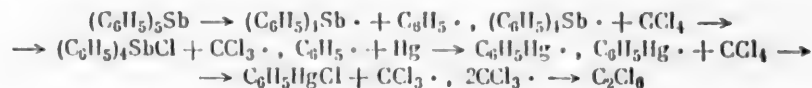
In carrying out the reaction of PPA with chloroform the basic products isolated were tetraphenylstibonium chloride and benzene, and a by-product was diphenyl; benzyldiene chloride was not found among the reaction products, although it could be expected according to the work of Wittig [5], the more so since PPA has a greater tendency to ionic reaction than does PPP. From these facts, the reaction can be represented by the following scheme, which agrees with the results obtained in studying the reaction of PPP with chloroform.



The reaction of PPA with carbon tetrachloride occurs in an analogous way to the above description and the results of this reaction are also analogous to those obtained in the reaction of PPP with carbon tetrachloride.



For confirmation of the formation of the phenyl radical in this reaction in the case of chloroform we used α, α' -diphenyl- β -trinitrophenylhydrazyl (the violet color of the solution turned yellow), and in the case of carbon tetrachloride, fixation of the radical on mercury. The latter reaction took place with excess mercury. Phenyl mercuric chloride was isolated quantitatively in the reaction product. The reaction takes place as follows.

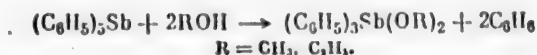


In the splitting of PPA in benzene we isolated the same products as in the thermal decomposition of PPA [2] in the absence of a solvent, namely, diphenyl and triphenylantimony.



Orienting experiments carried out with labeled benzene showed that diphenyl is formed without participation of the solvent, that is, here there is intramolecular splitting of PPA. PPP heated in benzene also splits into diphenyl and triphenyl phosphine, but the reaction is accompanied by formation of P-phenyldiphenylene phosphine and tar, which is not found in the case of PPA.

The reaction of PPA with aliphatic alcohols (methyl and ethyl), as in the case of PPP, occurs with splitting of two phenyl radicals. The reaction products are triphenylantimony dihydroxide and benzene.



Eighty % of the starting PPA reacts according to this equation. After treatment of the reaction mixture with alcoholic HCl we obtained tetraphenyl stibonium chloride (20%) as a by-product which shows that only one phenyl group takes part in the partial splitting. In the reaction of PPP with alcohols we did not find formation of derivatives of tetraphenyl phosphonium.

In conclusion we should remark that splitting of PPA in this solvent is analogous to splitting of PPP except that it occurs under more severe conditions (longer heating, higher temperatures) and is accompanied by side reactions.

EXPERIMENTAL

PPA was obtained by the method of Wittig [2] by the action of 1 N solution of lithium phenyl on antimony pentachloride etherate. After recrystallization from cyclohexane in a nitrogen atmosphere, m. p. 166°; the literature give m. p. 169-170° [2].

Thermal reaction with chloroform. Ten g of PPA and 25 ml of chloroform were heated in a sealed tube at 100° for 20 hours. After distillation of the solvent, the residue was distilled with steam. The benzene which distilled with the chloroform and steam was nitrated. We obtained 1.15 g (38% calculated on one phenyl) of *m*-dinitrobenzene, m. p. 87°; a sample mixed with the pure product gave no depression. In the steam distillation we isolated diphenyl (0.05 g), m. p. 68°. A sample mixed with pure diphenyl melted at 69°. From the water solution after steam distillation we isolated 6.5 g (76%) of tetraphenyl stibonium chloride with m. p. 201-202°, which by the action of potassium bromide in aqueous medium was converted to tetraphenyl stibonium bromide, m. p. 214°; a sample mixed with the pure compound obtained by the method of [6] melted at 213°. Individual substances could not be isolated from the tarry residue (2 g).

Photoreaction with chloroform. Three g of PPA and 15 ml of chloroform were irradiated in a quartz tube, diameter 20 mm, by ultraviolet light from a PRK-2 lamp for 50 hours. We isolated 1.8 g (70%) of tetraphenylstibonium chloride with m. p. 199-200° and a small amount of *m*-dinitrobenzene with m. p. 87°. A sample mixed with pure *m*-dinitrobenzene melted at 88°.

Thermal reaction with carbon tetrachloride. Five g of PPA and 20 ml of carbon tetrachloride were heated in a sealed tube at 100° for 25 hours. The solvent was distilled off. The residue was distilled with steam, and the first portions of the distillate contained carbon tetrachloride and chlorobenzene. This mixture was separated from the water and dried. Chlorobenzene was determined by the infrared absorption spectrum. In this were present all the sufficiently intense absorption bands of chlorobenzene with frequencies 700, 900, 1020, 1082, 1114, 1458, 1490, and 1600 cm^{-1} .

Diphenyl (0.1 g) distilled with the steam; m. p. 68°, a mixed sample with commercial diphenyl melted at 69°. The tetraphenyl stibonium chloride (3.9 g, 92%) had m. p. 201°. By the action of potassium bromide this was converted to the corresponding bromide with m. p. 212°.

Reaction with mercury in carbon tetrachloride. Five g of PPA, 20 g of metallic mercury, and 25 ml of carbon tetrachloride were energetically shaken in an atmosphere of nitrogen for 100 hours at room temperature. The solution was separated, and the residue, which contained finely divided mercury, was first treated with carbon tetrachloride to remove tetraphenyl stibonium chloride and then with hot alcohol to remove phenyl mercuric chloride. The tetraphenyl stibonium chloride was isolated in the amount of 3.2 g (74%) with m. p. 202°; a sample mixed with the chloride obtained in the reaction with chloroform gave no melting point depression. Phenyl mercuric chloride was isolated in the amount of 2.8 g (98%) with m. p. 247°; a sample mixed with the pure product melted at 248°.

Thermal reaction with methyl alcohol. Four g of PPA was heated with 15 ml of dry methyl alcohol in a sealed tube for 30 hours at 100°. The tube was opened, the solvent was distilled off and diluted with water and the benzene which separated was extracted with carbon tetrachloride and nitrated. We isolated 1.2 g of *m*-dinitrobenzene (49%, calculated on two phenyls) with m. p. 68°; a sample mixed with pure product gave no melting point depression. The residue was treated with alcohol saturated with hydrogen chloride; we isolated 2.7 g (87.5%) of triphenylantimony dichloride with m. p. 142°; a sample mixed with known triphenylantimony dichloride obtained by the method of [7] gave no melting point depression. The literature gives [8]: m. p. 143°. The residue after removal of the alcohol was treated with hot water and by the action of potassium bromide we isolated tetraphenyl stibonium bromide (0.29 g, 8%) with m. p. 209°; a sample mixed with a known bromide obtained according to [6] melted at 213°.

Thermal reaction with ethyl alcohol. a) We heated 4.450 g of PPA with 15 ml of anhydrous alcohol in a sealed tube for 40 hours at 100°. The solvent was distilled off and diluted with water; the benzene which separated was extracted with carbon tetrachloride and nitrated. We obtained 1.3 g (48%) of *m*-dinitrobenzene with m. p. 88°; a sample mixed with pure substance melted at 89°. The residue after removal of the solvent was treated with alcohol saturated with hydrogen chloride. We obtained 2.7 g (79%) of triphenylantimony dichloride with m. p. 141°; a sample mixed with known product had m. p. 142°. In the concentrated alcoholic solution we obtained 0.65 g (19%) of tetraphenyl stibonium chloride, m. p. 202°. For identification, this was converted to bromide by the action of potassium bromide. M. p. 205-210°; a sample mixed with pure bromide melted at 213°.

b) Four g of PPA was heated with 15 ml of anhydrous alcohol in a sealed tube for 30 hours at 100°. The solvent was distilled off, the residue was steam distilled. The first portion, and also the alcohol which distilled after the reaction were diluted with water. The benzene which separated was extracted with carbon tetrachloride and nitrated. We obtained 0.9 g (36.6%) of *m*-dinitrobenzene with m. p. 87°. The residue after distillation with steam was dissolved in glacial acetic acid and poured into a large amount of water, on which there precipitated 2.2 g (71%) of triphenylantimony dihydroxide with m. p. 206°; a sample mixed with known substance [9] melted at 211°. For further identification it was dissolved in alcohol and hydrogen chloride was passed through the solution; we isolated triphenylantimony dichloride with m. p. 142°; a sample mixed with known substance melted at 143°.

SUMMARY

1. Pentaphenylantimony when heated in benzene solution breaks down into diphenyl and triphenylantimony.
2. The reaction of pentaphenylantimony with chloroform and carbon tetrachloride occurs with breaking off of one phenyl group and formation of tetraphenyl stibonium chloride, benzene, and chlorobenzene in the case of carbon tetrachloride. The free radical nature of the reaction is shown in chloroform solution by the change in color of α, α' -diphenyl- β -trinitrophenylhydrazyl, and in carbon tetrachloride, by fixation of the radicals on mercury.
3. The reaction of pentaphenylantimony with alcohols occurs with splitting of two phenyl groups.
4. The reactions of pentaphenylantimony are analogous to the reactions of pentaphenylphosphorus, except that they occur under more severe conditions.

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THE SYNTHESIS OF ACYL DERIVATIVES OF HYDRAZIDES OF PYRIDINE AND FURAN CARBOXYLIC ACIDS

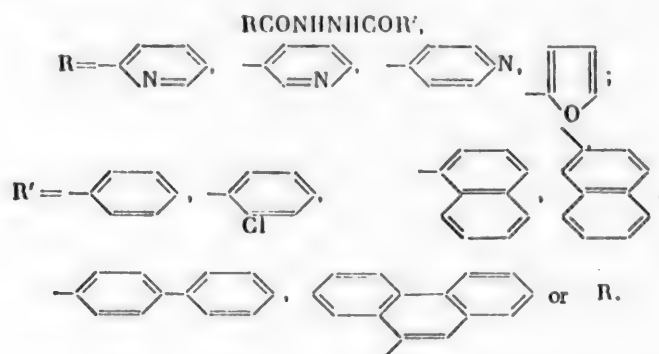
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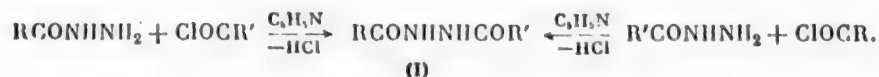
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pp. 3237-3239, October, 1960

Original article submitted July 6, 1959

At the present time acylated hydrazides of heterocyclic acids (1,2-diacylhydrazines) are finding wide use as physiologically active preparations [1, 2], and also as starting products for obtaining a number of new compounds [3, 4] used in scintillation techniques. In this work we have synthesized the undescribed acyl hydrazides of 2-, 3-, and 4-pyridine- and 2-furancarboxylic acids of the general formulas



These compounds were obtained by the reaction of equimolar amounts of the corresponding hydrazides with acid chlorides according to the well known scheme



We have found that the acyl hydrazides of heterocyclic acids are formed at room temperature in distinction from acyl derivatives of aromatic acid hydrazides where under similar conditions it is recommended to use heating [3]. The synthesis of acyl hydrazides of heterocyclic acids from acid chlorides and acid hydrazides at higher temperatures leads to formation along with the main reaction product (I) of diacyl hydrazide derivatives of the type RCONHN(COR)_2 (some aliphatic and aromatic diacyl hydrazides were described previously [5]); these on hydrolysis gave the monoacyl hydrazides again. In the synthesis of acyl hydrazides in boiling solvents we obtained along with the above mentioned products symmetrical 1,2-diaroylhydrazines [6].

As solvent for the synthesis of acyl hydrazides pyridine is usually used since it binds the hydrochloric acid formed in the reaction and this favors more complete utilization of the starting reagents and also the obtaining of acyl hydrazides of pyridine carboxylic acids as free bases. It should be noted, however, that this makes it more difficult to isolate the acyl hydrazides, due to their good solubility in pyridine. They are usually isolated

Acyl Hydrazides

No.	Name	M. P.	Yield, %	Empirical formula	%N	
					found	calc.
1	1-Benzoyl-2-(2-pyridoyl)-hydrazine	209-210°	78	C ₁₃ H ₁₁ O ₂ N ₃	17.25	17.43
2	1-Benzoyl-2-(3-pyridoyl)-hydrazine	258	37	C ₁₃ H ₁₁ O ₂ N ₃	17.43	17.43
3	1-(1-Naphthoyl)-2-(3-pyridoyl)-hydrazine	181.5-182.5	73	C ₁₇ H ₁₃ O ₂ N ₃	14.12	14.43
4	1-(2-Naphthoyl)-2-(3-pyridoyl)-hydrazine	168.5-169.5	95	C ₁₇ H ₁₃ O ₂ N ₃	14.10	14.43
5	1-(4-Biphenyloyl)-2-(3-pyridoyl)-hydrazine	250-251	86	C ₁₉ H ₁₅ O ₂ N ₃	13.21	13.24
6	1-(2-Chlorobenzoyl)-2-(3-pyridoyl)-hydrazine	148-149.5	48	C ₁₃ H ₁₀ O ₂ N ₃ Cl	15.15	15.27
7	1-(1-Naphthoyl)-2-(4-pyridoyl)-hydrazine	190.5-191.5	55	C ₁₇ H ₁₃ O ₂ N ₃	14.47	14.43
8	1-(2-Naphthoyl)-2-(4-pyridoyl)-hydrazine	211-212	50	C ₁₇ H ₁₃ O ₂ N ₃	14.20	14.43
9	1-(4-Biphenyloyl)-2-(4-pyridoyl)-hydrazine	224.5-225	73	C ₁₉ H ₁₅ O ₂ N ₃	13.14	13.24
10	1-(2-Furoyl)-2-(3-pyridoyl)-hydrazine	229-230	38	C ₁₁ H ₉ O ₃ N ₃	18.25	18.18
11	1-(2-Furoyl)-2-(4-pyridoyl)-hydrazine	238-240	42	C ₁₁ H ₉ O ₃ N ₃	17.82	18.18
12	1-(1-Naphthoyl)-2-(2-furoyl)-hydrazine	201-201.5	65	C ₁₆ H ₁₂ O ₃ N ₂	10.20	10.00
13	1-(2-Naphthoyl)-2-(2-furoyl)-hydrazine	220-221	91	C ₁₆ H ₁₂ O ₃ N ₂	10.31	10.00
14	1-(4-Biphenyloyl)-2-(2-furoyl)-hydrazine	216.5-218	79	C ₁₈ H ₁₄ O ₃ N ₂	9.23	9.15
15	1-(2-Furoyl)-2-(9-phenanthrenoyl)-hydrazine	220-221	62	C ₂₀ H ₁₄ O ₃ N ₂	8.54	8.48

by pouring the reaction mixture into 5-7 times its volume of water. In some cases for better precipitation of the product the reaction mixture is first diluted with ethanol or acetone to double the volume, and then treated as shown above. If the substance is difficult to precipitate, the excess solvent is distilled off in a vacuum, which, however, leads to considerable tarring of the product. The remaining pyridine and its hydrochloride are washed out with water. The resulting acyl hydrazides are crystallized from suitable organic solvents and also purified chromatographically on aluminum oxide using dioxane as the solvent. Isolation of the substances is carried out by dilution of the purified solution with 3-5 times its volume of ligroin.

As evidence for the structure of the synthesized acyl hydrazides (I) we have the counter syntheses in the scheme given above, by which the resulting compounds were identical in properties and elementary analysis.

All the acyl hydrazides described in this work were colorless, crystalline substances, easily soluble in acetone, dioxane, pyridine, ethanol, less easily in hot water, insoluble in benzene and ligroin. When heated in a vacuum or with phosphorus oxychloride they formed the corresponding 2,5-derivatives of 1,3,4-oxadiazole; they were hydrolyzed by the action of aqueous solutions of acids or alkalis on them. The acyl derivatives of the hydrazides of pyridine carboxylic acids gave salts with mineral acids.

EXPERIMENTAL •

1-Benzoyl-2-(2-pyridoyl)-hydrazine (1-benzoylhydrazide of picolinic acid). To a solution of 10 g (0.073

•L. A. Stepanenko took part in the experimental work.

mole) of 2-pyridine carboxylic (picolinic) acid hydrazide [7] in 100 ml of dry pyridine was slowly added with good stirring 10.2 g (0.073 mole) of benzoyl chloride (strong heating occurred). The resulting mass was stirred for two hours, then diluted with 200 ml of distilled water and allowed to stand for two hours. The precipitated reaction product was filtered off, washed on the filter with water, and dried at 70°. Yield 13.9 g (78%), m. p. 203-204°. For further purification the substance was dissolved in dioxane and submitted to chromatographic purification on aluminum oxide ("for chromatography").

The substance was precipitated from dioxane solution by diluting it with ligroin and was 1-benzoyl-2-(2-pyridoyl)-hydrazine, a colorless, crystalline substance with m. p. 209-210°.

Found %: N 17.25. $C_{13}H_{11}O_2N_3$. Calculated %: N 17.43.

By analogous methods, considering the methods described above, we synthesized all the other acyl hydrazides of heterocyclic acids which are shown in the table.

SUMMARY

We have synthesized fifteen undescribed acyl derivatives of hydrazides of pyridine- and furancarboxylic acids and have studied their properties.

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THE SYNTHESIS OF SOME HETEROCYCLIC DERIVATIVES OF 1,3,4-OXADIAZOLE

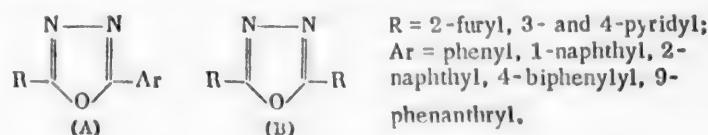
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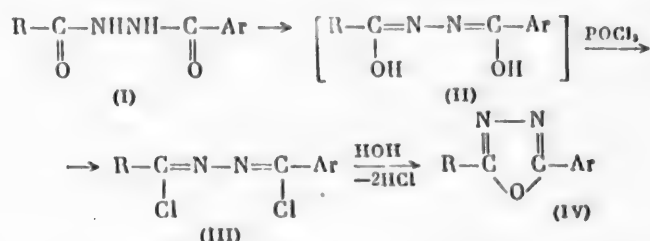
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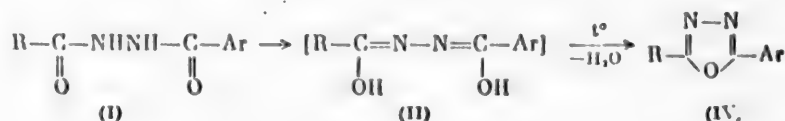
It has recently been shown that 2,5-diaryl derivatives of 1,3,4-oxadiazole are the best media known in the literature of liquids for scintillators, and there has also been a study of the effect of some aromatic radicals on their scintillation properties [1-3]. Data on the action of heterocyclic substituents on scintillation derivatives of 1,3,4-oxadiazole are scarcely found in the literature. Therefore, for the study of this question, we have synthesized a series of new heterocyclic derivatives of 1,3,4-oxadiazole of the general formulas (A) and (B).



These compounds were obtained by cyclizing the corresponding diacyl hydrazines (I) [4] by the well known scheme [5-7].



However, the preparation of heterocyclic derivatives of 1,3,4-oxadiazole is complicated as compared to compounds which contain only aromatic radicals [5, 6] because of their considerably lower chemical stability and the difficulty isolating them from the reaction mass. This is especially characteristic for derivatives of oxadiazole which contain even one pyridine radical, since they give hydrochlorides with the hydrogen chloride formed during the reaction. Therefore in such cases the preparation of a substance as the free base is carried out by neutralization of its hydrochloride with aqueous ammonia or diethylamine. Some of the above mentioned compounds were also synthesized by heating the diacyl hydrazines (I) to 180-200° in a vacuum according to the following scheme [8].



In derivatives of 1,3,4-oxadiazole obtained by both processes from the same diacyl hydrazine, the properties and elementary analysis for nitrogen were analogous.

Purification of these compounds was carried out by crystallization from a suitable solvent and by chromatography on aluminum oxide.

The heterocyclic derivatives of 1,3,4-oxadiazole synthesized in the present work were colorless, crystalline substances, soluble in benzene, toluene, pyridine, alcohol, acetone, and dioxane; soluble with difficulty in ligroin and water. They dissolved in hydrochloric acid with formation of salts which were also obtained by passing hydrogen chloride through their benzene solutions. When they were heated with aqueous solutions of mineral acids and alkalis, they underwent hydrolysis.

EXPERIMENTAL*

Synthesis of 2,5-di(3-pyridyl)-1,3,4-oxadiazole. A mixture of 2.5 g of 1,2-di(3-pyridoyl)-hydrazine [4] and 40 ml of phosphorus oxychloride was boiled in a flask with a reflux condenser for 20 hours. Then about 30 ml of POCl_3 was distilled from the reaction mixture and the residue was carefully poured into a beaker which contained 100 ml of water with ice (strong heating took place). The resulting mass stood overnight, after which, with good cooling, it was neutralized to litmus with concentrated ammonia (80-85 ml) to a clearly alkaline reaction. The precipitated product after ice cooling was filtered, washed on the filter with 5 ml of distilled water, and dried. After chromatographic purification on aluminum oxide using benzene as the solvent we obtained pure 2,5-di(3-pyridyl)-1,3,4-oxadiazole with a yield of 0.53 g (23%), m. p. 188°.

Synthesis of 2-(2-naphthyl)-2-(4-pyridyl)-1,3,4-oxadiazole. Thirteen g of 1-(2-naphthoyl)-2-(4-pyridoyl)-hydrazine [4] and 65 ml of POCl_3 were boiled for 11 hours and left overnight. The resulting mixture was carefully poured into 400 ml of water with energetic stirring and cooling. The resulting hot solution was filtered from the insoluble precipitate and cooled with ice. The precipitate was filtered, washed on the filter with a small amount of water, and dried. The yield of 2-(2-naphthyl)-5-(4-pyridyl)-1,3,5-oxadiazole hydrochloride was 9.76 g, m. p. 225° (with decomposition). To obtain the free base we boiled the substance with 200 ml of alcohol to which in the course of 30 minutes we added 20 ml of diethylamine. After 30 minutes, the whole mass was poured into 400 ml of water. After good cooling, the precipitate was filtered off, washed on the filter with water (100 ml) and dried; yield 7.2 g. Then the benzene solution of the substance was purified chromatographically on aluminum oxide with later precipitation from the solvent by addition of ligroin, and then was twice recrystallized from benzene with the use of activated charcoal. Yield 1.82 g (15%), m. p. 177.5-178°.

Synthesis of 2-(2-furyl)-5-(3-pyridyl)-1,3,4-oxadiazole. Seventeen g of 1-(2-furoyl)-2-(3-pyridoyl)-hydrazine [4] and 80 ml of POCl_3 were boiled for eight hours. The excess phosphorus oxychloride was distilled in a vacuum and the residue was poured into 180 ml of water. After cooling, the mass was neutralized with ammonia (50 ml) to a neutral reaction to litmus, and the precipitate was filtered, washed with water (50 ml) and dried; yield 14.4 g. This substance was dissolved in acetone (200 ml), treated with activated charcoal, twice passed through a layer of aluminum oxide, and precipitated with ligroin (600 ml), m. p. 130°. Then the product was again dissolved in acetone (50 ml), 150 ml of distilled water was added, and the mixture was well cooled. The precipitate of 2-(2-furyl)-5-(3-pyridyl)-1,3,4-oxadiazole was filtered, washed on the filter with water, and dried; yield 2.5 g (16%), m. p. 130-131°.

Synthesis of 2-(2-furyl)-5-(2-naphthyl)-1,3,4-oxadiazole. A mixture of 1-(2-furoyl)-2-(2-naphthoyl)-hydrazine (47 g) [4] and 190 ml of phosphorus oxychloride was boiled under reflux for five hours. After cooling, the reaction mass was distilled in a vacuum to remove 110 ml of POCl_3 and the residue was slowly poured into 450 ml of water with stirring. The precipitate was filtered off, washed with water on the filter, and dried. After recrystallization from benzene with later chromatography of a dioxane-benzene solution (1 : 1.5) over aluminum oxide (precipitating with ligroin) we obtained 2-(2-furyl)-5-(2-naphthyl)-1,3,4-oxadiazole with a yield of 18.8 g (43%), m. p. 144.5-145°.

In an analogous way we obtained the other heterocyclic derivatives of 1,3,4-oxadiazole shown in the table.

* L. A. Stepanenko took part in the experimental work.

Heterocyclic Derivatives of 1,3,4-Oxadiazole

No.	Name	Melting point	Yield, %	Empirical formula	%N	
					found	calculated
1	2,5-Di-(3-pyridyl)-1,3,4-oxadiazole	188°	23	C ₁₂ H ₈ ON ₄	24.70	24.99
2	2-Phenyl-5-(3-pyridyl)-1,3,4-oxadiazole	126—126.5	44	C ₁₃ H ₉ ON ₃	18.87	18.83
3	2-(1-Naphthyl)-5-(3-pyridyl)-1,3,4-oxadiazole	135—136	34	C ₁₇ H ₁₁ ON ₃	15.22	15.38
4	2-(4-Biphenyl)-5-(3-pyridyl)-1,3,4-oxadiazole	172.5—173.5	15	C ₁₉ H ₁₃ ON ₃	13.97	14.04
5	2-Phenyl-5-(4-pyridyl)-1,3,4-oxadiazole	145	20	C ₁₃ H ₉ ON ₃	18.76	18.83
6	2-(2-Furyl)-5-(3-pyridyl)-1,3,4-oxadiazole	130—131	16	C ₁₁ H ₇ O ₂ N ₃	20.01	19.71
7	2-(2-Furyl)-5-(4-pyridyl)-1,3,4-oxadiazole	148—149	11	C ₁₁ H ₇ O ₂ N ₃	19.44	19.71
8	2-(2-Furyl)-5-(1-naphthyl)-1,3,4-oxadiazole	104—105	41	C ₁₆ H ₁₀ O ₂ N ₂	10.92	10.68
9	2-(2-Furyl)-5-(2-naphthyl)-1,3,4-oxadiazole	144.5—145	43	C ₁₆ H ₁₀ O ₂ N ₂	10.81	10.68
10	2-(2-Furyl)-5-(1-biphenyl)-1,3,4-oxadiazole	135—135.5	34	C ₁₈ H ₁₂ O ₂ N ₂	9.75	9.72
11	2-(2-Naphthyl)-5-(3-pyridyl)-1,3,4-oxadiazole	157.5—158.5	11	C ₁₇ H ₁₁ ON ₃	15.45	15.38
12	2-(4-Biphenyl)-5-(4-pyridyl)-1,3,4-oxadiazole	173—174	20	C ₁₉ H ₁₃ ON ₃	14.26	14.04
13	2-(2-Furyl)-5-(9-phenanthryl)-1,3,4-oxadiazole	243—243.5	20	C ₂₀ H ₁₂ O ₂ N ₂	9.03	8.86
14	2-(1-Naphthyl)-5-(4-pyridyl)-1,3,4-oxadiazole	143—144	14	C ₁₇ H ₁₁ ON ₃	15.66	15.38
15	2-(2-Naphthyl)-5-(4-pyridyl)-1,3,4-oxadiazole	177.5—178	15	C ₁₇ H ₁₁ ON ₃	15.28	15.38

SUMMARY

We have synthesized fifteen undescribed heterocyclic derivatives of 1,3,4-oxadiazole and studied some of their properties.

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* Original Russian pagination. See C. B. translation.

REACTIONS OF CHLORINE-CONTAINING TELOMERS OF DIENE HYDROCARBONS.

IV. REACTIONS OF 1-CHLORO-5,5-DIMETHYL-2-HEXENE AND 1,3-DICHLORO- 5,5-DIMETHYL-2-HEXENE WITH SODIUM ACETOACETIC AND SODIUM MALONIC ESTERS

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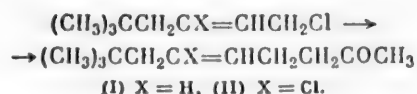
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In order to study the possibility of use in organic synthesis of the adducts of tertiary halogen derivatives with diene compounds, we have studied the reaction of 1-chloro-5,5-dimethyl-2-hexene (the adduct of tertiary butyl chloride to divinyl) and 1,3-dichloro-5,5-dimethyl-2-hexene (the adduct of the same halogen derivative to chloroprene) with sodium acetoacetic and sodium malonic esters.

It was shown previously that these halogen derivatives easily form the corresponding aldehydes in the Sommelet reaction [1]. The reaction with sodium acetoacetic ester has also been studied for other telomers [2].

The experiments showed that under ordinary conditions from both of the chlorides studied and sodium acetoacetic ester there was obtained an unsaturated ketone with a quaternary carbon atom at the end of the chain according to the scheme:



The resulting ketones were colorless oils with a pleasant odor, insoluble in water. They easily formed crystalline products with hydrazine derivatives.

In the infrared spectra of ketones the carbonyl group accounts for two frequencies 1717 and 1727 cm^{-1} of medium intensity, the double bond for the weak frequencies 1627 and 1656 cm^{-1} respectively. In the spectrum of ketone (I) there is an intense frequency of deformation CH oscillation of the grouping $-\text{CH}=\text{CH}-$ (trans) at 970 cm^{-1} and the analogous frequency for the vinyl group is absent. Hence in the condensation there is no rearrangement of the reaction centers, and the isomeric ketone with the vinyl group is not formed. In the spectrum of ketone (II) the analogous oscillation in the grouping $-\text{CCl}=\text{CH}-$ is evidently the medium intensity frequency 840 cm^{-1} . In both spectra there is an intense frequency characteristic for ketones about 1360 cm^{-1} . The frequencies 1160 and 1240 cm^{-1} are evidently connected with the presence of the quaternary carbon atom (Fig. 1, curves 1 and 2).

In carrying out the condensation with sodium acetoacetic ester there is usually obtained a small high-boiling fraction. Judging by the infrared spectrum the higher fraction obtained with substance (I) is an unsaturated ketone (the spectrum has frequencies 1717 and 1640 cm^{-1}) and contains the grouping $-\text{CH}=\text{CH}-$ (there is a frequency 971 cm^{-1}) (Fig. 1, curve 3). Evidently this product comes from reaction of the chloride with sodium acetoacetic ester in the ratio 2 : 1. The substance was not further investigated.

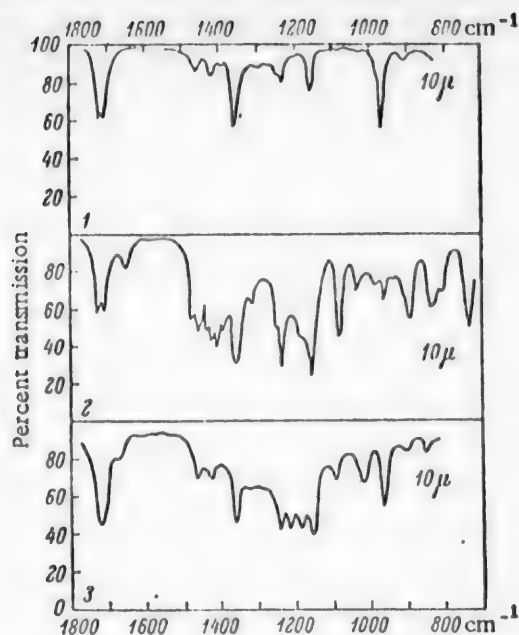
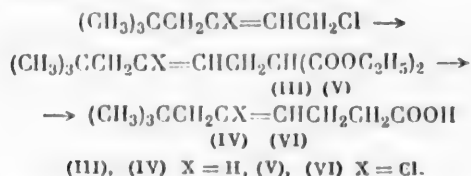


Fig. 1. Infrared transmission spectra; 1) 2,2-dimethyl-4-nonen-8-one, 2) 4-chloro-2,2-dimethyl-4-nonen-8-one, 3) fraction 120-124° (4 mm) from residue from distillation of first ketone.

In the condensation of the same chlorides with sodium malonic ester we obtained the corresponding alkene malonic esters, but in poor yields.



EXPERIMENTAL

2,2-Dimethyl-4-nonen-8-one. To sodium acetoacetic ester obtained from 5.35 g of metallic sodium, 170 ml of anhydrous alcohol, and 35 g of freshly distilled acetoacetic ester we added in the course of 1.5 hours with stirring and cooling 34 g of 1-chloro-5,5-dimethyl-2-hexene. The mixture was stirred 1.5 hours at 40-50° (water bath) and allowed to stand overnight. Then after heating at 60-70° for 1.5 hours the mixture was treated with 100 ml of 10% NaOH and heating was continued for three hours more at the same temperature. The mixture was

acidified to clear separation into layers with hydrochloric acid, the upper, slightly colored layer was separated, washed with bicarbonate solution and water, dried over Na_2SO_4 , and vacuum distilled (10 mm). We thus obtained the following fractions: 1st to 86° , 4.7 g; 2nd $86-95^\circ$, 19 g; 3rd $95-120^\circ$, 2.7 g; 4th $120-122^\circ$ (4 mm) 2.6 g. Residue 7.8 g.

By repeated distillation of the second fraction, it came over almost entirely within 1° . The yield of the ketone was about 50%.

2,2-Dimethyl-4-nonen-8-one had the following constants.

B. p. $88.5-89.5^\circ$ (10 mm), d_4^{20} 0.8346, n_D^{20} 1.4394, MR 53.03; calc. 52.54.

Found %: C 78.34, 78.50; H 12.04, 12.08. M 164.6, 165.4. $\text{C}_{11}\text{H}_{20}\text{O}$. Calculated %: C 78.51; H 11.98. M 168.3.

Infrared spectrum: 907 (w), 970 (s), 1161 (m), 1200 (w), 1238 (m), 1365 (s), 1390 (w), 1406 (w), 1430 (w), 1464 (w), 1627 (w), 1717 (s), 1724 (s) cm^{-1} .

The semicarbazone had m. p. $124.5-125^\circ$ (from aqueous alcohol). Fine, colorless needles.

Found %: N 18.26, 18.22. $\text{C}_{12}\text{H}_{23}\text{ON}_3$. Calculated %: N 18.65.

The 2,4-dinitrophenylhydrazone had m. p. $101-101.5^\circ$ (from alcohol). Fine orange rods.

Found %: N 15.68, 15.95. $\text{C}_{17}\text{H}_{24}\text{O}_4\text{N}_4$. Calculated %: N 16.08.

4-Chloro-2,2-dimethyl-4-nonen-8-one. From 120 ml of anhydrous alcohol, 2 g of metallic sodium, 15 ml of acetoacetic ester, and 15 g of 1,3-dichloro-5,5-dimethyl-2-hexene we obtained about 18 g of reaction product from which vacuum fractionation gave 9.4 g (56%) of 4-chloro-2,2-dimethyl-4-nonen-8-one.

B. p. $113-115^\circ$ (10 mm), d_4^{20} 0.9619, n_D^{20} 1.4608, MR 57.80; calc. 57.41.

Found %: C 65.58, 65.67; H 9.53, 9.63; Cl 17.69, 17.42. M 193.6, 194.1. $\text{C}_{11}\text{H}_{19}\text{OCl}$. Calculated %: C 65.17; H 9.44; Cl 17.49. M 202.

Infrared spectrum: 742 (m), 814 (w), 840 (m), 898 (m), 912 (v. w), 928 (v. w), 967 (m), 994 (v. w), 1062 (w), 1089 (m), 1160 (s), 1238 (s), 1252 (m), 1321 (w), 1359 (s), 1398 (w), 1412 (s), 1429 (m), 1444 (m), 1465 (m), 1480 (w), 1656 (w), 1717 (m), 1727 (m) cm^{-1} .

The semicarbazone had m. p. $140-140.5^\circ$ (from aqueous alcohol). Colorless fine needles.

Found %: N 16.61, 16.84. $\text{C}_{12}\text{H}_{22}\text{ON}_3\text{Cl}$. Calculated %: N 16.18.

The 2,4-dinitrophenylhydrazone had m. p. $95-95.5^\circ$ (from alcohol). Fine yellow needles.

Found %: N 14.58, 14.49. $\text{C}_{17}\text{H}_{23}\text{O}_4\text{N}_4\text{Cl}$. Calculated %: N 14.63.

7,7-Dimethyl-4-octenoic acid (IV). To sodium malonic ester obtained from 2.75 g of sodium and 27 g (one and a half fold excess) of freshly distilled malonic ester in 75 ml of anhydrous alcohol was added dropwise with mechanical stirring 18 g of 1-chloro-5,5-dimethyl-2-hexene. Reaction occurred with considerable heating. After addition of all the chloride, stirring was continued for five hours more and the bath temperature was gradually raised to 75° . Then the cooled reaction mixture was poured into water and the reaction product was extracted with ether. The ether extract was washed several times with water, the ether was distilled off, and the residue was fractionated in a vacuum (2-3 mm). We thus obtained the following fractions: 1st $33-40^\circ$, 11.4 g; 2nd $40-54^\circ$, 4 g; 3rd $54-60^\circ$, 9.9 g (malonic ester); 4th $104-108^\circ$, 4.7 g [diester (III), yield 14%].

For 5,5-dimethyl-2-hexenylmalonic ester (III) we found: b. p. $143-145.5^\circ$ (10 mm), d_4^{20} 0.9589, n_D^{20} 1.4420, MR 74.45; calc. 74.31.

Found %: C 66.28, 66.25; H 9.71, 9.72. $\text{C}_{15}\text{H}_{26}\text{O}_4$. Calculated %: C 66.63; H 9.69.

Infrared spectrum: 772 (v. w), 856 (w), 972 (m), 1033 (s), 1095 (m), 1144 (s), 1184 (s), 1223 (s), 1256 (s), 1298 (s), 1328 (s), 1367 (s), 1391 (m), 1446 (m), 1466 (m), 1736 (s), 1747 (s) cm^{-1} .

Two g of ester (III) was saponified by heating with 6 g of NaOH in 17 ml of water to solution of the oily layer. The solution was acidified with 20 ml of concentrated HCl and the resulting acid was extracted with ether. Yield of acid (IV) about 1 g (80%).

For 7,7-dimethyl-2-octenoic acid (IV) we found: b. p. 135-137° (13 mm), d_4^{20} 0.9001, n_D^{20} 1.4460, MR 50.44; calc. 49.45.

Found %: C 70.36, 70.89; H 11.01, 10.87; H_{act} , 0.57. $C_{10}H_{18}O_2$. Calculated %: C 70.55; H 10.66; H_{act} , 0.59.

Infrared spectrum: 728 (v. w), 776 (v. w), 828 (w), 932 (s), 968 (s), 1017 (m), 1080 (m), 1144 (m), 1209 (s), 1240 (s), 1281 (s), 1327 (s), 1365 (s), 1391 (s), 1411 (s), 1428 (s), 1463 (s), 1473 (s), 1708 (v. s) cm^{-1} .

From the acid by the action of thionyl chloride in benzene and then of ammonia we obtained the amide with m. p. 110-110.5° (from aqueous alcohol).

Found %: N 8.28, 8.11; H_{act} , 1.17. $C_{10}H_{19}ON$. Calculated %: N 8.28; H_{act} , 1.19.

We should remark that in some experiments when undistilled ester (III) was saponified, along with acid (IV) we obtained a carbonyl compound which formed a 2,4-dinitrophenylhydrazone with m. p. 179-180.5°.

Found %: N 18.37, 18.37.

5-Chloro-7,7-dimethyl-4-octenoic acid (VI). Using an analogous method we obtained from 5.1 g of sodium, 35.4 g of malonic ester, and 40 g of 1,3-dichloro-5,5-dimethyl-2-hexene an oil, from which vacuum distillation gave 3-chloro-5,5-dimethyl-2-hexenylmalonic ester (V) with a yield of 22.5%.

B. p. 150-152° (5 mm), d_4^{20} 1.0402, n_D^{20} 1.4555, MR 79.57; calc. 79.18.

Found %: C 59.65, 59.36; H 8.52, 8.51; Cl 11.93, 11.99. $C_{15}H_{25}O_4Cl$. Calculated %: C 59.10; H 8.27; Cl 11.63.

Infrared spectrum: 699 (w), 740 (w), 785 (w), 816 (w), 835 (w), 858 (m), 885 (w), 957 (w), 1034 (s), 1094 (s), 1152 (s), 1180 (s), 1193 (s), 1232 (s), 1260 (s), 1330 (s), 1369 (s), 1392 (s), 1448 (s), 1468 (s), 1657 (m), 1737 (s) cm^{-1} .

From the saponification product of ester (V) by vacuum distillation we isolated a fraction 135-155° (4 mm), most of which crystallized in the receiver. Easily soluble in alcohol, ether, benzene, chloroform, and dioxane.

5-Chloro-7,7-dimethyl-4-octenoic acid (VI) had m. p. 47-47.5° (from aqueous dioxane).

Found %: C 59.22, 59.07; H 8.30, 8.57; Cl 17.68, 17.44. Acid equiv. 206.3 $C_{10}H_{17}O_2Cl$. Calculated %: C 58.67; H 8.37; Cl 17.32. Acid equiv. 204.7.

Infrared spectrum: (5% solution in CCl_4): 725 (v. w), 830 (w), 904 (m), 931 (m), 1033 (w), 1083 (w), 1092 (w), 1122 (v. w), 1160 (w), 1210 (s), 1248 (s), 1282 (s), 1336 (s), 1413 (s), 1428 (s), 1469 (s), 1656 (m), 1706 (s) cm^{-1} .

The acid amide of (VI) had m. p. 72.5-73° (from aqueous dioxane).

Found %: N 7.18, 6.82; Cl 17.71, 17.59. $C_{10}H_{18}ONCl$. Calculated %: N 6.88; Cl 17.40.

Besides acid (VI), in the saponification of ester (V) we obtained other products, especially an unsaturated carbonyl compound (in the infrared spectrum there were frequencies 1659 and 1726 cm^{-1}) which formed a 2,4-dinitrophenylhydrazone with m. p. 125-128°.

Found %: N 16.79, 16.96.

This substance was not further investigated.

SUMMARY

1. We have studied the reaction of 1-chloro-5,5-dimethyl-2-hexene and 1,3-dichloro-5,5-dimethyl-2-hexene with sodium acetoacetic and sodium malonic esters.

2. We have showed that in this way can be obtained the corresponding ketones and acids, 2,2-dimethyl-4-nonen-8-one, 4-chloro-2,2-dimethyl-4-nonen-8-one, 7,7-dimethyl-4-octenoic acid, and 5-chloro-7,7-dimethyl-4-octenoic acid.

3. We have studied the infrared spectra of these ketones and acids and obtained derivatives: for the ketones, crystalline semicarbazones and 2,4-dinitrophenylhydrazones, for the acids, crystalline amides.

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HYDROGENATION OF UNSATURATED COMPOUNDS IN THE PRESENCE OF COLLOIDAL PALLADIUM

XIV. SOME CHARACTERISTICS OF THE HYDROGENATION OF DISUBSTITUTED ALLENE HYDROCARBONS

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A palladium catalyst, colloidal or on a carrier, is often used in laboratory practice as a selective catalyst in hydrogenation. However, in the case of hydrocarbons with different unsaturated bonds the selectiveness of adding hydrogen is not always high. Diene hydrocarbons are hydrogenated over palladium in all possible directions and the catalyst causes rearrangements, shifts of the double bonds in the middle of the carbon chain [1]. Alkenyl-

acetylenes are hydrogenated selectively on the acetylene bond; in the case of vinylalkylacetylenes and vinylacetylene itself the dienes formed are hydrogenated to a considerable extent at the same time as the vinylacetylenes, and in the hydrogenation products appear many olefins, even with partial use of the starting substances [2-4].

The characteristics of the hydrogenation of allene hydrocarbons have not been determined to a sufficient extent in the literature.

We have investigated the hydrogenation of seven disubstituted allenes whose formulas are given in Table 1. We have also hydrogenated four hydrocarbons of the vinyl- and isopropenylallenes.

Here we established that the hydrogenation of allene hydrocarbons occurs at an increasing rate up to the absorption of half the calculated amount of hydrogen, after which the reaction goes very slowly (Fig. 1). The end products of the hydrogenation are the corresponding saturated hydrocarbons [5].

The infrared spectra of the hydrogenation products of the allenes after half absorption of hydrogen show the almost complete absence of allene compounds in them (by the frequencies 875 and 1960 cm^{-1}). Thus, hydrogenation occurs strictly selectively (Fig. 2).

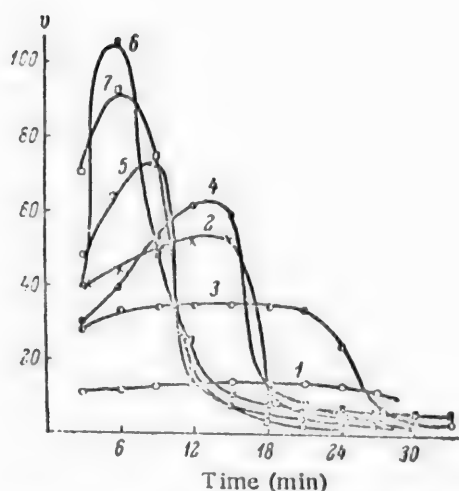


Fig. 1. Curves of rate of hydrogenation of allenes. 1) 3,4-Octadiene; 2) 3,4-nonadiene; 3) 3,4-decadiene; 4) 7-methyl-2,3-octadiene; 5) 7-methyl-3,4-octadiene; 6) 6,6-dimethyl-2,3-heptadiene; 7) 7,7-dimethyl-3,4-octadiene.

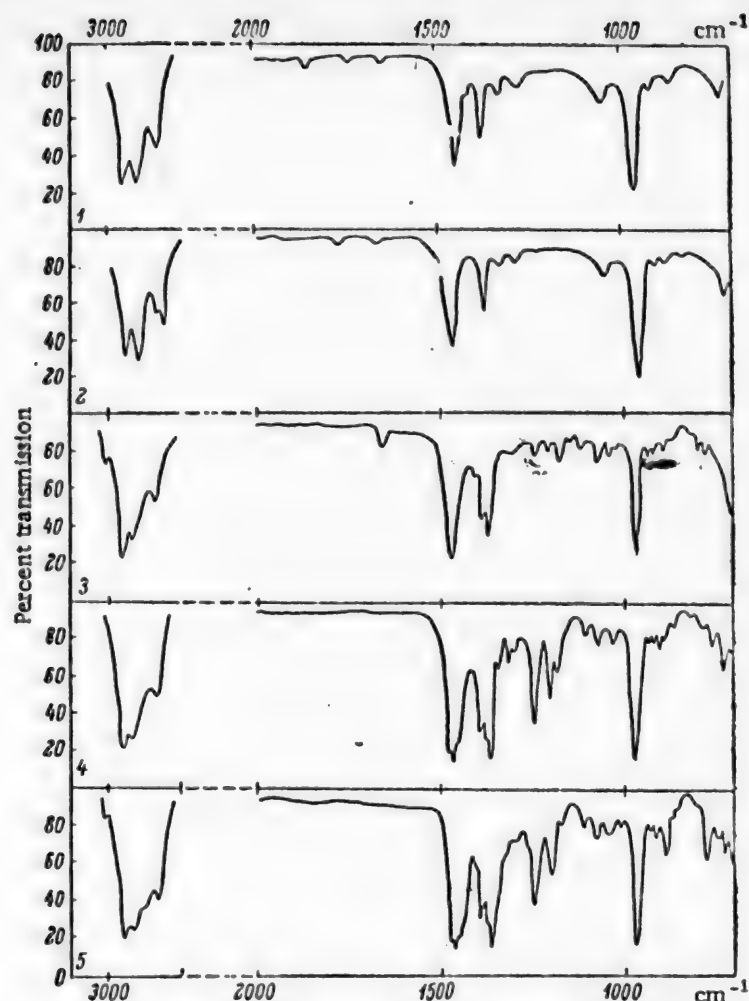


Fig. 2. Infrared transmission spectra of the hydrogenation products of allene hydrocarbons (in the ratio hydrocarbon: hydrogen = 1 : 1. 1) 3,4-Octadiene; 2) 3,4-nonadiene; 3) 7-methyl-2,3-octadiene; 4) 6,6-dimethyl-2,3-heptadiene; 5) 7,7-dimethyl-3,4-octadiene.

The course of the curves for rate of hydrogenation depends on the structure of the hydrocarbons. For hydrocarbons with an iso structure it is characteristic to have a more rapid rise in the rate of hydrogenation (especially if they contain a tertiary butyl radical), than for hydrocarbons with a normal structure. No characteristic differences in the rate of hydrogenation of 2,3- and 3,4-dienes were observed (Fig. 1). The effect of alkyl radicals is probably connected with an increased polarity of the system. At the same time, since in the hydrocarbons which we studied branching of the chain occurred only on the second carbon atom with respect to the allene system, spacial hindrance could not occur.

Ozonization of the hydrogenation products from 3,4-nonadiene with half the amount of hydrogen showed that both possible olefins were formed at the same time. In the decomposition of the ozonide propionic, butyric, valeric and caproic acids were obtained.

Hydrogenation of vinyl- and isopropenylallenes also takes place with increasing speed up to the addition of almost two molecules of hydrogen, after which the rate of the reaction falls sharply (Fig. 3). The later molecule of hydrogen adds very slowly.

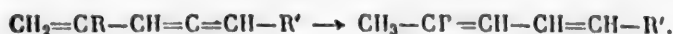
After addition of the first mole of hydrogen to 8-methyl-1,3,4-nonatriene we did not find in the infrared spectrum of the hydrogenation product the frequencies of allene (890 and 1960 cm^{-1}) and vinyl (988 cm^{-1}) groups and at the same time there appeared the frequency of deformation oscillation of a disubstituted ethylene group

TABLE 1

Summarized Hydrogenation of Allenes and Alkenylallenes

Starting hydro-carbon	Amount of hydrogen absorbed (in ml) in the time (minutes)											Pressure (in. mm)	Temperature (°C)	Calculated amount of hydrogen (in ml)
	3	6	9	12	15	18	21	24	27	30	60	120		
3,4-Octadiene	11	22	35	49	63	77	90	103	116	130	227	252	732.5	510
3,4-Nonadiene	39	82	132	183	236	247	253	258	261	263	270	276	732.5	510
3,4-Decadiene	28	61	94	127	161	195	228	252	258	262	278	—	744.5	501
7-Methyl-2,3-octadiene	28	68	121	183	243	255	263	268	273	276	306	358	729.3	511
7-Methyl-3,4-octadiene	47	108	180	242	255	263	269	275	280	284	324	388	755.5	495
6,6-Dimethyl-2,3-heptadiene	102	207	255	273	282	290	297	304	311	316	364	431	767	487
7,7-Dimethyl-3,4-octadiene	70	162	236	251	260	266	271	276	281	285	317	355	759.3	488
1,3,4-Octatriene	105	297	402	426	445	456	466	475	483	490	—	—	756.7	738
1,3,4-Decatriene	104	333	492	522	539	551	561	570	577	583	—	—	750.5	735
2-Methyl-1,3,4-octatriene	195	393	440	463	479	492	503	513	522	530	580	636	766.8	724

(965 cm⁻¹). Hence the first molecule of hydrogen adds to this hydrocarbon selectively in the 1,4-position according to the scheme



It is possible that the known role is here played by the isomerizing action of palladium catalysts in hydrogenation.

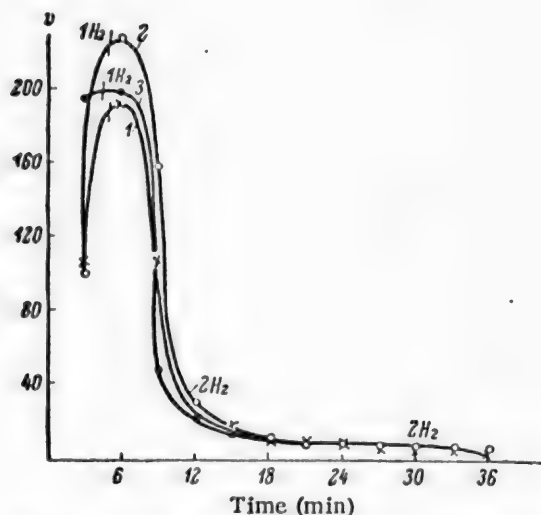


Fig. 3. Curves of rate of hydrogenation for alkenylallenes; 1) 1,3,4-octatriene; 2) 1,3,4-decatriene; 3) 2-methyl-1,3,4-octatriene.

In the infrared spectra of analogous products of partial hydrogenation of 2-methyl-1,3,4-octatriene the characteristic frequencies of the isopropenyl and allene groupings have not completely vanished, although they are markedly weakened compared to the starting hydrocarbons (Fig. 4). As in the first case, the frequency 965 cm⁻¹ appears in the spectrum. Hence, the replacement of hydrogen in position 2 by methyl shifts the hydrogenation according to the scheme given above, probably because there is some difficulty in adsorption of the conjugated grouping of the starting hydrocarbon on the catalyst. However, as before there is preferential addition in the 1,4-position.

Thus, as a result of this study it has been established that hydrogenation of disubstituted allenes occurs selectively and most resembles the hydrogenation of acetylenes with terminal acetylene groupings. In the case of alkenylallenes the direction of hydrogenation depends to a considerable extent on the structure of the hydrocarbons.

TABLE 2

Constants of the Hydrogenation Products of Allene and Alkenylallene Hydrocarbons (in the Ratio Hydrocarbon : Hydrogen = 1 : 1)

Starting hydrocarbon	B. p.	d_4^{20}	n_D^{20}	Characteristic frequencies (cm ⁻¹)		
				$\nu_{\text{C}=\text{C}=\text{C}}$	$\nu_{\text{C}=\text{C}}$	δ_{CH}
3,4-Octadiene*	122–123°	0.7161	1.4108	None	1658	965
3,4-Nonadiene	145–148	0.7266	1.4160	"	1658	967
7-Methyl-2,3-octadiene	138.5–140	0.7276	1.4170	"	1656	966
6,6-Dimethyl-2,3-heptadiene	130–131.5	0.7164	1.4078	"	1660	971
7,7-Dimethyl-3,4-octadiene	154.5–156	0.7302	1.4170	"	1660	971
8-Methyl-1,3,4-nonatriene	163–165	0.7473	1.4320	"	1600–1647	971
2-Methyl-1,3,4-octatriene	146–148	0.7480	1.4400	1960 (traces)	1600–1645	968

* Hydrogenation took place with absorption of 1.1 mole H₂.

** The constants of the mixture of olefins were close to those given in the literature [8, 9] for the individual hydrocarbons, the possible hydrogenation products of allenes and alkenylallenes, and are given in the table.

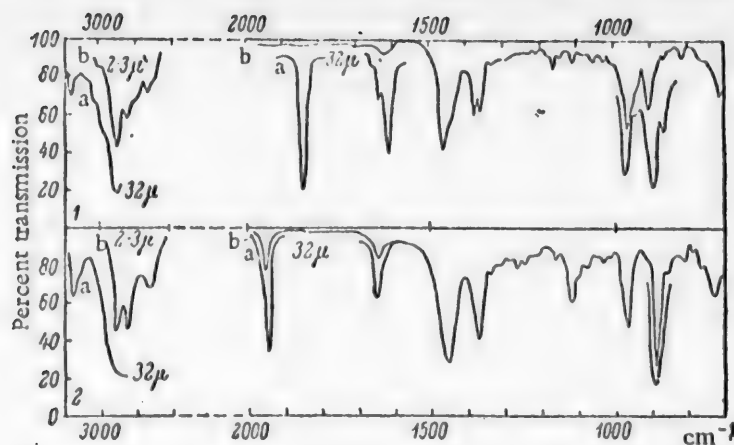


Fig. 4. Infrared transmission spectra of hydrogenation products of alkenyllallenes (in the ratio hydrocarbon : hydrogen = 1 : 1). 1^a) 8-Methyl-1,3,4-nonatriene; 1^b) its hydrogenation product; 2^a) 2-methyl-1,3,4-octatriene; 2^b) its hydrogenation product.

EXPERIMENTAL

The allene hydrocarbons were obtained by addition of lithium alkyls to vinylalkylacetylenes, and, judging by the infrared spectra, did not contain any considerable quantity of admixtures of isomers with a different arrangement of double bonds [5, 6]. Vinyl- and isopropenylallenes were obtained by analogous methods from divinylacetylene and isopropenylvinylacetylene [7].

Hydrogenation was carried out in an ordinary reactor at a rate of 120 oscillations per minute. To a solution of 0.01 mole of hydrocarbon in 30 ml of methanol was added 1 ml of colloidal palladium with a content of 1 mg of palladium in 1 ml. In the case of the vinylallenes the amount of catalyst was increased to 3 ml, since at smaller amounts in some cases poisoning occurred. The experimental data are given in Table 1 and Figs. 1 and 3.

For the five allene hydrocarbons we carried out hydrogenation of large samples with half the calculated amount of hydrogen. We thus obtained a mixture of 3- and 4-alkenes with the constants given in Table 2. Thus, for example, 6.09 g of 3,4-octadiene was hydrogenated in 30 ml of methanol in the presence of 5 ml of colloidal palladium to absorption of 1323 ml of hydrogen (774.6 mm, 19°). The reaction mixture was diluted with water and distilled until the hydrocarbon stopped coming over. The distillate was dried with CaCl_2 , the hydrocarbon was separated and distilled. We obtained 5.5 g of substance (90%). The constants are given in Table 2. They are close to those given in the literature for 3- and 4-octenes [8].

The infrared spectra of the hydrocarbon mixtures are given in Fig. 3. The spectra do not show frequencies for allene groupings. The double bond corresponds to a very weak valence frequency of 1661 cm^{-1} and a strong deformation frequency of 965 cm^{-1} , which shows the presence of the grouping $-\text{CH}=\text{CH}-$ (trans).

The hydrogenation products of 3,4-nonadiene were ozonized. We ozonized 2.9 g of substance in 20 ml of ethyl chloride. The ozonide was decomposed by heating with 15% hydrogen peroxide. The aldehydes were oxidized with potassium permanganate. The resulting acids were extracted in an extractor with a stirrer using ether and after the ether had been distilled off they were distilled in a microcolumn. We thus obtained fractions which corresponded to all four possible acids in their properties. The acids were converted to their silver salts and the latter were analyzed.

Silver propionate (recrystallized from water). Found %: Ag 59.01. $\text{C}_3\text{H}_5\text{O}_2\text{Ag}$. Calculated %: Ag 59.61.

Silver butyrate. Found %: Ag 55.33. $\text{C}_4\text{H}_7\text{O}_2\text{Ag}$. Calculated %: Ag 55.24.

Silver valerate. Found %: Ag 49.85. $\text{C}_5\text{H}_9\text{O}_2\text{Ag}$. Calculated %: Ag 51.63.

Silver caproate. Found %: C 32.94; H 5.42. $\text{C}_6\text{H}_{11}\text{O}_2\text{Ag}$. Calculated %: C 32.30; H 4.94.

For the two alkenylallene hydrocarbons we carried out hydrogenation of larger samples in a ratio of hydrocarbon : hydrogen = 1 : 1. The constants and characteristic frequencies of the hydrogenation products are given in Table 2.

SUMMARY

1. We have studied some regularities in the hydrogenation of disubstituted allene hydrocarbons: 3,4-octadiene, 3,4-nonadiene, 3,4-decadiene, 7-methyl-2,3-octadiene, 7-methyl-3,4-octadiene, 6,6-dimethyl-2,3-heptadiene, and 7,7-dimethyl-3,4-octadiene.
2. We have shown that addition of the first mole of hydrogen usually goes with increasing rate, after which the hydrogenation process is greatly slowed. In the case of hydrocarbons with an iso structure this rule is shown more sharply.
3. We have showed that hydrogenation of allenes goes selectively, and with absorption of half the calculated amount of hydrogen there is formed a mixture of olefins with double bonds in the 2-, 3-, or 4-positions. Allene hydrocarbons react fully here.
4. Hydrogenation of alkenylallenes (1,3,4-octatriene, 1,3,4-decatriene, 2-methyl-1,3,4-octatriene and 8-methyl-1,3,4-octatriene) occurs in an analogous way: after absorption of about two moles of hydrogen the rate of the reaction falls steeply. Allene hydrocarbons and hydrocarbons with terminal double bonds vanish entirely or to a considerable extent after absorption of the first mole of hydrogen.

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EXPERIMENTAL SYNTHESIS IN THE DIPYRRYLMETHENE SERIES

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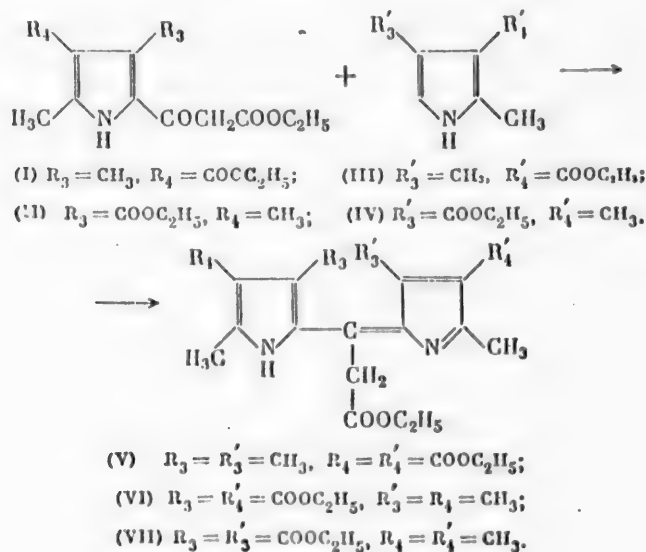
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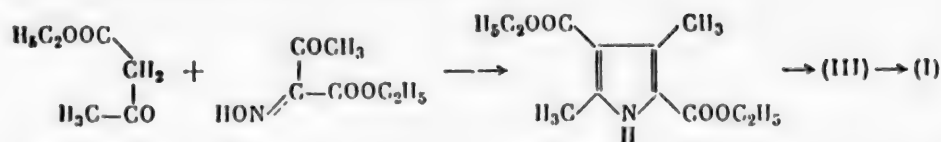
Original article submitted July 20, 1959

The mesocarbomethoxymethylpyrromethenes are of the greatest interest in the synthesis of porphyrins of the type of pheophorbide a, pheophorphyrin a₅, pheophytin, and chlorophyll. There is a well known synthesis for this class of compounds, which consists of oxidizing the dipyrrolylpropionic esters which are formed by the condensation of formyl acetic ester [1], the acid chloride of monoethyl malonic ester [2], a monoester of tartaric acid [3] or of one of the pyrrolylacrylic acids [1] with pyrroles which are unsubstituted in the α - or β -position. However, the majority of these methods can be used to prepare only symmetric dipyrrolylpropionic esters. The synthesis of unsymmetric meso-substituted dipyrrolylmethenes presents considerable problems.

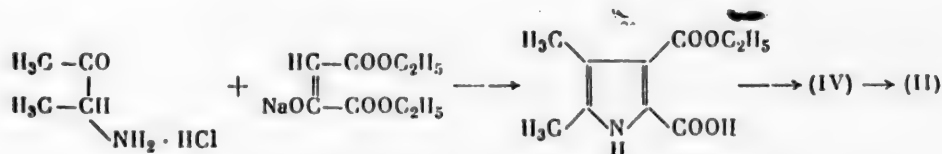
In the present work we studied the preparation of meso-substituted dipyrrolylmethenes through the corresponding keto-compounds. In the condensation of pyrrolylsubstituted β -ketoacids with pyrroles having the α -position free, meso-substituted pyrromethenes are formed. The reaction was studied for the case of the ethyl ester of β -(2,4-dimethyl-3-carbomethoxypyrrolyl-5)- β -ketopropionic acid (I), as well as the ethyl ester of β -(2,3-dimethyl-4-carbomethoxypyrrolyl-5)- β -ketopropionic acid (II), which were condensed with 2,4-dimethyl-3-carbomethoxypyrrole (III) and 2,3-dimethyl-4-carbomethoxypyrrole (IV).



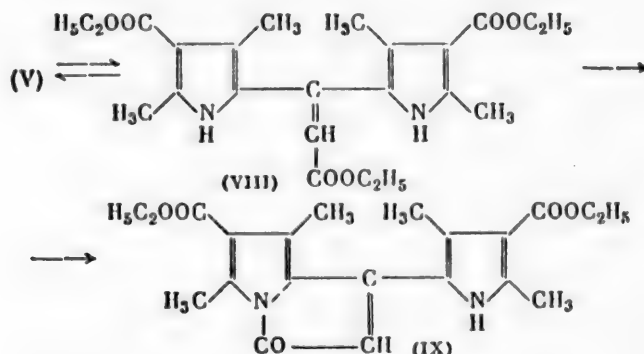
The initial pyrroles were prepared by Knorr's synthesis [4].



In the 2,4-dimethyl-3,5-dicarbethoxypyrrole, the α -carbethoxy group is hydrolyzed with alcoholic alkali decarboxylation is carried out, and then the 2,4-dimethyl-3-carbethoxypyrrole (III) is condensed with cyanoacetic ester to give compound (I). The 2,3-dimethyl-4-carbethoxypyrrole (IV), prepared by the reaction in alkaline solution between oxalic ester and aminobutanone hydrochloride, with subsequent decarboxylation, is converted by condensation with cyanoacetic ester to the ethyl ester of β -(2,3-dimethyl-4-carbethoxypyrrol-5)- β -ketopropionic acid (II).



The condensation of (I) and (II) with (III) and (IV) was carried out in chloroform or benzene in the presence of phosphorus pentoxide. In the condensation of (I) with (III), the 3,3', 5,5' - tetramethyl-4,4' - dicarbethoxymesocarbethoxymethylpyrromethene (V) separated out in the form of an amorphous violet colored powder. On slight alkalization of the alcoholic solution of dipyrromethene the violet color changes to cinnamon red. The same color change is observed on passing a benzene solution of dipyrromethene (V) through an aluminum oxide column. Here there is a rearrangement of the methene system (V) into the tautomeric ethylene form (VIII), which after separation of alcohol forms the lactam (IX).



The possibility of such transformation was demonstrated by Treibs and co-workers [6]. The structure of 3,3' -5,5' - tetramethyl-4,4' -dicarbethoxymesocarbethoxymethylpyrromethene (V) and the lactam (IX) is supported by infrared spectra data. The condensation of (II) with (III), and (II) with (IV), leads to dipyrromethenes having a bright yellow color. A bright red color from compound (VI) and a violet color from compound (VII) are observed in acid solution, as well as in the substance freshly precipitated from acid solution, but on standing and recrystallization it is easily changed to bright yellow. Thus, for the methenes under consideration, the ethylene form seems to be the more stable one.

EXPERIMENTAL

Ethyl ester of β -(2,4-dimethyl-3-carbethoxypyrrol-5)- β -ketopropionic acid (I). Dissolve 5 gm. 2,4-dimethyl-3-carbethoxypyrrole (III) (m. p. 75-76°) and 7 gm. of the ethyl ester of cyanoacetic acid in 25 ml of absolute ether, and after cooling to -15°, pass a stream of dry HCl through for one hour. Let stand for three hours. Remove the ether in vacuum, add 50 ml of water to the residue, and heat for five minutes on a water bath (60-65).

On cooling, long needle shaped crystals precipitate out. Separate and recrystallize from alcohol. Yield 7.25 gm. (86.2%). M. p. 140.5 - 142°.

Found %: C 59.49; H 6.82; N 4.85. $C_{14}H_{19}O_5N$. Calculated %: C 59.78; H 6.76; N 4.98.

2,4-Dimethyl-3-carbethoxy-5-carboxypyrrole. Add four grams of metallic sodium to 30 ml of alcohol. After all the sodium has reacted, pour in 3.5 ml of water and add a solution of 40 gm. 2,4-dimethyl-3,5-di-carbethoxypyrrole (m. p. 134 - 135°) in 150 ml of alcohol, and heat under a reflux condenser for two hours. Distill off the alcohol in vacuum. Dissolve the residue in 250 ml of water, filter, and after cooling with ice, separate the free acid by acidifying with 20% sulfuric acid. Yield 32.1 gm. (90.6%). M. p. 202° (decomp.)-[5].

3,3', 5,5' - Tetramethyl-4,4' -dicarbethoxymesocarbethoxymethylpyrromethene (V). Dissolve one gram of the ethyl ester of β -(2,4-dimethyl-3-carbethoxypyrrol-5)- β -ketopropionic acid (m. p. 140.5 - 142°) and 0.6 gm. 2,4-dimethyl-3-carbethoxypyrrole (m. p. 75 - 76°) in 50 ml anhydrous benzene, add two grams of phosphorus pentoxide, and boil for three hours. The solution takes on a red-violet color. Decant the benzene solution. Extract the residue with anhydrous benzene (three times, 20 ml each). Wash the collected benzene extract with water to the disappearance of acid reaction with Congo red. Distill off the solvent in vacuum. Recrystallize the residue from 1 : 1 alcohol and water. Yield 0.65 gm. (43.9%). M. p. 70-72°.

Found %: C 64.10; H 6.81; N 6.83. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.20; H 6.98; N 6.53.

After washing the mixture of structural isomers with benzene, separate the dipyrromethene with m. p. 184 - 186°.

Found %: C 64.25; H 6.80; N 6.50. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.20; H 6.98; N 6.53.

3,3', 5,5' - Tetramethyl-4,4' -dicarbethoxymesolactampyrromethene (IX). a) Dissolve 0.5 gm. 3,3' -, 5,5' -tetramethyl-4,4' -dicarbethoxymesocarbethoxymethylpyrromethene in 10 ml of alcohol, and add five drops of a 10% solution of alkali. This changes the violet color to cinnamon red. Add the alkaline solution to 20 ml of water, and extract the substance with ether. Remove solvent. Wash the residue several times with benzene. Yield 0.28 gm. (62.6%). M. p. 132 - 134°.

Found %: C 65.58; H 6.32; N 6.99. $C_{21}H_{24}O_5N_2$. Calculated %: C 65.60; H 6.25; N 7.29.

b) Dissolve 0.15 gm. 3,3', 5,5' -tetramethyl-4,4' -dicarbethoxymesocarbethoxymethylpyrromethene in 25 ml of dry benzene, and pass through a column filled with aluminum oxide. The material is adsorbed in the upper part of the column. Elute with a 1 : 1 mixture of benzene and alcohol. From the brownish fraction, which makes up most of the volume, extract a brick red substance. Yield 0.076 gm. (50.6%). After washing with the petroleum ether m. p. 132 - 134°.

Found %: C 65.61; H 6.18; N 7.20. $C_{21}H_{24}O_5N_2$. Calculated %: C 65.60; H 6.25; N 7.29.

Ethyl ester of β -(2,3-dimethyl-4-carbethoxypyrrol-5)- β -ketopropionic acid (II). Dissolve 3.02 gm. 2,3-dimethyl-4-carbethoxypyrrole (IV) (m. p. 110 - 111°) and four grams of the ethyl ester of cyanoacetic acid in 40 ml of absolute ether. After thorough cooling for three hours, pass through a stream of dry HCl, and let stand overnight. Remove the ether, and dissolve the residue in 200 ml of water. Filter the aqueous solution, and heat to 50 - 60° for 20 minutes. An oil separates out, which solidifies on cooling. Separate the precipitate, recrystallize from alcohol, and dry in a vacuum dessicator. Yield 3.26 gm. (61.5%). M. p. 56 - 57°.

Found %: C 59.83; H 6.5; N 5.04. $C_{14}H_{19}O_5N$. Calculated %: C 59.75; H 6.80; N 4.98.

4,5,3', 5' - Tetramethyl-3,4' -dicarbethoxymesocarbethoxymethylpyrromethene (VI). Dissolve 0.38 gm. of the ethyl ester of β -(2,3-dimethyl-4-carbethoxypyrrol-5)- β -ketopropionic acid (m. p. 56 - 57°) and 0.22 gm. 2,4-dimethyl-3-carbethoxypyrrole (m. p. 75 - 76°) in 10 ml of anhydrous chloroform, add 0.76 gm. phosphorus pentoxide in small portions, and stir for four hours at room temperature. The reaction mixture takes on a red-violet color. Neutralize with a 1% ammonia solution. The color of the solution changes to cinnamon red. Wash the chloroform solution with water. Distill off the solvent in vacuum. Treat the residue five times with 10 ml each of petroleum ether. Distill off the solvent in vacuum. Treat the residual oil with absolute ether. This gives a yellow precipitate. Filter it off, recrystallize from alcohol, and dry in a vacuum dessicator. Yield 0.26 gm. (44.6%). M. p. 181 - 182°.

Found %: C 64.25; H 7.03; N 6.51. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.2; H 6.98; N 6.53.

Dissolve 50 gm. of the pyrromethene with m. p. 181–182° in two ml of anhydrous chloroform and pass through a stream of dry HCl. The solution becomes violet-red. Evaporate the chloroform. This gives a red amorphous powder. M. p. 70–87°. On standing in air, or on treatment with solvents, the red color disappears. A new yellow substance is formed. M. p. 181–182°.

4,5,4',5'-Tetramethyl-3,3'-dicarboethoxymesocarboethoxymethylpyrromethene (VII). Dissolve 0.38 gm. of the ethyl ester of β -(2,3-dimethyl-4-carboethoxypyrryl-5)- β -ketopropionic acid (m. p. 56–57°) and 0.22 gm. 2,3-dimethyl-4-carboethoxypyrrole in 10 ml of anhydrous chloroform, add 0.76 gm. phosphorus pentoxide in small portions, and stir for four hours at room temperature. The reaction mixture takes on a red-violet color. Neutralize with a 1% ammonia solution. The color changes to orange. Wash the chloroform solution with water. Distill off the solvent in vacuum. Rub the residual oil into a powder with petroleum ether, recrystallize from petroleum ether and dry in a vacuum desiccator. Yield 0.29 gm. (50%). M. p. 159–160°.

Found %: C 64.34; H 6.71; N 6.68. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.2; H 6.98; N 6.53.

SUMMARY

1. A method has been worked out for synthesizing mesosubstituted pyrromethenes, which makes it possible to prepare unsymmetric dipyrromethenes.

2. It is shown that depending upon the pH of the medium, the methenes can exist in either the pyrromethene or the ethylene form. The relative stability of the two forms depends upon the character and position of the substituents in the pyrrole rings.

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EXPERIMENTAL SYNTHESSES IN THE FIELD OF THE COCAINES

VII. PREPARATION OF THE RACEMIC STEREOISOMERIC ALKALOIDS COCAINE, PSEUDOCOCAINE, ALLOCOCAINE, and ALLOPSEUDOCOCAINE

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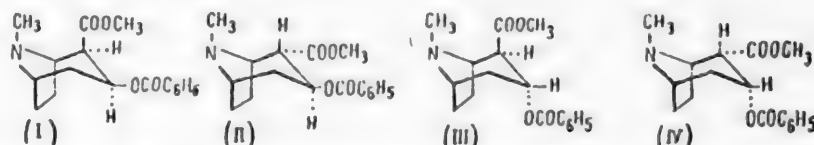
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Natural (-)-cocaine belongs to the tropine group of alkaloids, and has the composition 2- β -carbomethoxy-tropine (I).

The presence of asymmetric carbon atoms in the molecule, as well as the nonplanar structure of the piperidine ring, makes possible the existence of four racemic stereoisomeric forms: cocaine, pseudococaine, allococaine, and allospseudococaine, and eight optically active forms (I-IV and the corresponding enantiomers) [1-3].



R. Willstätter and E. Bode [4] succeeded in synthesizing racemic pseudococaine (II). A drawback of their method, the starting point of which was cycloheptane, was the large number of steps required, and the low yields obtained. Further, in this work, R. Willstätter was unable to prepare either natural cocaine or its corresponding racemate.

R. Robinson [5] condensed succindialdehyde with methylamine and acetonedicarboxylic acid to obtain tropinone, and from it tropine.

A variation of this reaction was carried out by R. Willstätter and co-workers [6] in the condensation of succindialdehyde with methylamine and the dipotassium salt of acetonedicarboxylic acid, which gave the methyl ester of tropinone-3-carboxylic-2 acid. Resolution of the tropinone carboxylic ester with subsequent benzoylation gave racemic pseudococaine and racemic cocaine (I). The levorotatory form of the latter was found to be identical with natural levo-cocaine.

K. Zeile and W. Schulz [7] have reported the synthesis of the third racemic cocaine (III) (semihydrate m. p. 156-158°). In this work, as well as in the paper of R. Willstätter and co-workers [6], to which the authors refer, no method is given for obtaining the third ecgonine, which does not facilitate reproducing the synthesis.

Over the course of several months in the same year, 1956, S. Findlay prepared the third and fourth racemic cocaines. Findlay's work was published in the form of a letter to the editor. No details of the synthesis are given, and the constants given for the third racemic ester of ecgonine (m. p. 81.5-83.5°), and the third racemic cocaine (m. p. 82-84°) are for the unhydrated bases, and thus do not agree with the constants of the corresponding

compounds prepared by Zeile and Schulz. In a recently published paper dealing with the methyl ester of tropinone-3-carboxylic-2 acid, S. Findlay [8] describes the methyl ester of the third racemic ecgonine as a liquid.

It should be noted that the conditions under which the experiments were carried out are given by the authors in the most general terms, and no answer is given to the question of resolution of the methyl ester of tropinone-3-carboxylic-2 acid or the preparation of the isomeric cocaine.

In the present paper we describe the benzylation of our previously [9] synthesized methyl esters of racemic stereoisomeric tropinol-3-carboxylic-2 acids and the preparation of the bases of the corresponding isomeric cocaine and their hydrochlorides and picrates.

EXPERIMENTAL

(±)-Cocaine. Base. Heat a solution of 4 gm. of the methyl ester of ecgonine in 36 ml anhydrous benzene, stirring for 10 hours at 96–100° with 7 ml benzoyl chloride in the presence of 1.6 gm. soda. When the reaction is complete, distill off the benzene in vacuum at 30° (20 mm). Cool the residue to 0°, add 40 ml of ice water, acidify with hydrochloric acid (Congo), extract the benzoic acid and the rest of the benzoyl chloride with ether (three times 20 ml each). Neutralize the aqueous solution at 0–2° with a 20% aqueous solution of ammonia (phenolphthalein). An oil separates out, which crystallizes rapidly. Separate the cocaine base, wash with ice water and dry. Yield 3.7 gm. (60.7%). M. p. 79.5–80.5° (from absolute ether).

Found %: C 67.28, 67.19; H 6.83, 6.92; N 4.72. $C_{17}H_{21}O_4N$. Calculated %: C 67.31; H 6.98; N 4.62.

Hydrochloride. M. p. 185–186°, def. 183°.

Found %: C 60.39; H 6.50; N 4.35. $C_{17}H_{21}O_4N \cdot HCl$. Calculated %: C 60.09; H 6.52; N 4.12.

Picrate. M. p. 210–212°, def. 205°.

Found %: C 51.86; H 4.49; N 10.47. $C_{23}H_{24}O_{11}N_4$. Calculated %: C 51.89; H 4.54; N 10.52.

(±)-Pseudococaine. Base. Heat 2.2 gm. of the methyl ester of pseudoeconine for 10 hours with 4.4 gm. benzoyl chloride at 96–100°. Wash the resulting crystalline mass of pseudococaine hydrochloride from the residual benzoyl chloride with ether, dissolve in 20 times its volume of ice water, filter and neutralize with ammonia. A quickly crystallizing oil is formed. Separate the pseudococaine base and wash with ice water. Yield 2.1 gm. (62.7%). M. p. 80–81.5° (from petroleum ether).

Found %: C 67.32; H 6.93; N 4.58. $C_{17}H_{21}O_4N$. Calculated %: C 67.31; H 6.98; N 4.62.

A sample of a mixture of pseudococaine (m. p. 80–81.5°) with cocaine (m. p. 79.5–80.5°) has m. p. 65–71°.

Hydrochloride. M. p. 212–213°, def. 210° (from anhydrous methyl alcohol).

Found %: C 60.20; H 6.66; N 4.27. $C_{17}H_{21}O_4N \cdot HCl$. Calculated %: C 60.09; H 6.52; N 4.12.

A sample of a mixture of pseudococaine hydrochloride (m. p. 212–213°, def. 210°) with cocaine hydrochloride (m. p. 185–186°, def. 183°), has m. p. 180–181°, def. 177°.

Picrate. M. p. 194–196°, def. 190° (from anhydrous methyl alcohol).

Found %: C 51.73; H 4.73; N 10.25. $C_{23}H_{24}O_{11}N_4$. Calculated %: C 51.89; H 4.54; N 10.52.

A sample of a mixture of pseudococaine picrate (m. p. 194–196°, def. 190°) with cocaine picrate (m. p. 210–212°, def. 205°) has m. p. 176–188°, def. 174°.

(±)-Allococaine. Base. Heat 0.4 gm. of the methyl ester of alloecgonine (prepared from one gram of the picrate of the methyl ester of alloecgonine with m. p. 126–131°, def. 125°) with 0.7 ml benzoyl chloride in benzene (3.6 ml) at 96–100° for 10 hours. The separation is carried out the same as in the preparation of cocaine. The allococaine base separates in form of a dense yellowish oil. Dry in vacuum desiccator. Yield 0.26 gm. (42.7%).

Hydrochloride. Hygroscopic crystals.

Found %: C 60.26; H 6.88; N 4.10. $C_{17}H_{21}O_4N \cdot HCl$. Calculated %: C 60.09; H 6.52; N 4.12.

Picrate. M. p. 130.5-132°, def. 128°.

Found %: C 51.63; H 4.64; N 10.87. $C_{23}H_{24}O_{11}N_4$. Calculated %: C 51.89; H 4.54; N 10.52.

A sample of a mixture of allococaine picrate (m. p. 130.5-132°, def. 128°) with the picrate of the methyl ester of allococaine (m. p. 126-131°, def. 125°) has m. p. 113-118°, def. 110°, with cocaine picrate (m. p. 210-212°, def. 205°) it has m. p. 125-182°, def. 122°, with pseudococaine picrate (m. p. 194-196°, def. 190°) it has m. p. 124-140°, def. 122°.

(±)-Allopseudococaine. Base. Heat 0.7 gm. of the methyl ester of allopseudoecgonine (prepared from 1.5 gm. of the picrate of the methyl ester of allopseudoecgonine with m. p. 196-198°, def. 195°) with 1.2 ml benzoyl chloride in benzene (6.3 ml) at 96-100° for 10 hours. The separation is carried out the same as in the preparation of cocaine. The allopseudococaine base separates in the form of a rapidly crystallizing oil. Yield 0.1 gm. (deducting the recovered methyl ester of allopseudoecgonine 26.3%). M. p. 83-84°, def. 81.5° (from absolute ether).

Found %: C 67.00; H 7.26; N 4.85. $C_{17}H_{21}O_4N$. Calculated %: C 67.26; H 6.98; N 4.62.

A sample of a mixture of allopseudococaine (m. p. 83-84°, def. 81.5°) with cocaine (m. p. 79.5-80.5°) has m. p. 60-67°, def. 57°, with pseudococaine (m. p. 80-81.5°) it has m. p. 59-63°, def. 55°.

Hydrochloride. M. p. 177-178°, def. 176°.

Found %: C 59.74; H 6.38; N 4.31. $C_{17}H_{21}O_4N \cdot HCl$. Calculated %: C 60.09; H 6.52; N 4.12.

A sample of a mixture of allopseudococaine hydrochloride (m. p. 177-178°, def. 176°) with cocaine hydrochloride (m. p. 185-186°, def. 183°) has m. p. 174-175°, def. 172°, with pseudococaine hydrochloride (m. p. 212-213°, def. 210°) it has m. p. 174-175°, def. 172.5°.

Picrate. M. p. 172-174°, def. 170°.

Found %: C 51.84; H 4.22; N 10.84. $C_{23}H_{24}O_{11}N_4$. Calculated %: C 51.89; H 4.54; N 10.52.

A sample of a mixture of allopseudococaine picrate (m. p. 172-174°, def. 170°) with cocaine picrate (m. p. 210-212°, def. 205°) has m. p. 167-171°, def. 160°, with pseudococaine picrate (m. p. 194-196°, def. 190°) it has m. p. 169-171°, def. 162°, with allococaine picrate (m. p. 130.5-132°, def. 128°) has m. p. 119-146°, def. 116°.

Methyl ester of allopseudotropinol-3-carboxylic-2 acid. After separating the allopseudococaine, saturate the ammoniacal solution with potash and extract the methyl ester of allopseudococaine with chloroform. Removal of the solvent gives a bright yellow, slowly crystallizing oil. Yield 0.45 gm. M. p. 81-83°, def. 79° (from petroleum ether).

Found %: C 60.02; H 8.20; N 6.94. $C_{10}H_{17}O_3N$. Calculated %: C 60.28; H 8.59; N 7.02.

A sample of a mixture of the methyl ester of allopseudococaine (m. p. 81-83°, def. 79°) with the methyl ester of pseudococaine (m. p. 128-130°) has m. p. 70-102°, def. 68°, with allopseudococaine (m. p. 83-84°, def. 81.5°) it has m. p. 57-64°, def. 55°.

Picrate. M. p. 195-198°, def. 194°.

Found %: N 12.9. $C_{16}H_{20}O_{10}N_4$. Calculated %: N 13.08

A sample of a mixture of the picrate of the methyl ester of allopseudoecgonine (m. p. 195-198°, def. 194°), prepared from the methyl ester of allopseudoecgonine separated from the mother solution after benzoylation, with the picrate of the original methyl ester of allopseudoecgonine (m. p. 196-198°, def. 195°) has m. p. 195-198°.

SUMMARY

1. A method has been worked out for benzoylation of the methyl esters of the racemic stereoisomeric tropinol-3-carboxylic-2 acids to give the corresponding isomeric compounds: cocaine, pseudococaine, allococaine, and allopseudococaine.

2. The bases of the racemic isomeric cocaines and their hydrochlorides and picrates were prepared.

3. The base and the picrate of the methyl ester of allopseudoecgonine were prepared.

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*Original Russian pagination. See C. B. translation.

INVESTIGATION OF SIMPLE ESTERS WITH ALLYL POSITION OF THE DOUBLE BOND

VII. AN ALLYL ESTER OF SALICYLALDEHYDE IN THE GRIGNARD REACTION

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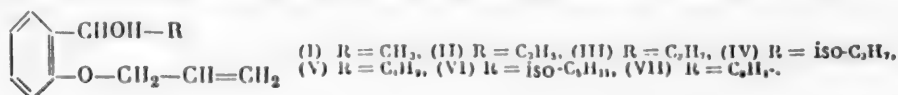
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The reaction of salicylaldehyde and its methyl and ethyl esters with alkyl and arylmagnesium bromide proceeds normally. This is also true for methyl and *p*-anisole magnesium iodide. The corresponding oxy- and alkyloxyphenyl substituted secondary alcohols are obtained in good yield [1-12]. However, with ethyl and propylmagnesium iodide the products of the reaction turn out to be derivatives of ethylene [13-15]. These are doubtless formed as a result of dehydration of the alcohols initially formed by the action of the Grignard reagent [16], or are formed by reaction with magnesium iodide.

In the present paper we prepared alcoholic esters from an allyl ester of salicylaldehyde and methylmagnesium iodide, ethyl, propyl, isopropyl, *n*-butyl, and isoamylmagnesium bromide, as well as octyl-2-magnesium bromide. In all cases the corresponding alkyl-(*o*-allyloxyphenyl)-carbinols were obtained.



EXPERIMENTAL

The allyl ester of salicylic aldehyde was prepared by Claisen's [17] well known method.

B. p. 114.5-115.5° (1 mm), 136-138° (12 mm), n_D^{20} 1.5527, d_4^{20} 1.0938, M_R^D 47.38; Calc. 45.97.

With dimedone it forms a bright yellow crystalline addition product with m. p. 186° (from 50% alcohol).

Preparation of alkyl-(*o*-allyloxyphenyl)-carbinols. The organic magnesium compounds were prepared by the usual method, adding the corresponding alkyl halide to magnesium in absolute ether in molar proportions. The next day, 0.5 mol of allyl ester of salicylic aldehyde in ether solution was added to the organic magnesium compound cooled to 0°, and allowed to stand at room temperature, after which the reaction mixture was cooled to -5-0° and decomposed with an aqueous solution of ammonium chloride. The ether extracts of the reaction products were dried with magnesium sulfate, or better - by the addition of a small quantity of potash. Then the solvent was distilled off, and the alcoholic ester was distilled over in vacuum.

It should be noted that if the quantity of allyl ester of salicylic aldehyde is increased, it does not enter completely into the reaction, and only contaminates the alkyl-(*o*-allyloxyphenyl)-carbinols. The latter are bright yellow liquids, insoluble in water, readily soluble in ether, benzene, and other organic solvents.

The physical constants and the analytical data for the alcoholic esters prepared are given in the table.

Properties of Alkyl-(o-allyloxyphenyl)-carbinols

Name of alcoholic Ester	Boiling point (pres- sure in mm)	n_D^{20}	d_4^{20}	MRD		Found (%)		Empirical formula	Calcu- lated (%)		M		Yield (%)
				found	calcu- lated	C	H		C	H	found	calcu- lated	
1-(o-Allyloxyphenyl)- ethanol-1 (I)	141.5° (6)	1.5323	1.0389	50.46	52.10	73.95	8.11	$C_{11}H_{14}O_2$	74.15	7.87	166.5	172	86.3
1-(o-Allyloxyphenyl)- propanol-1 (II)	142—146 (4)	1.5340	1.0407	57.34	56.72	75.06	8.42	$C_{12}H_{16}O_2$	75.00	8.33	192.3	192	67.2
1-(o-Allyloxyphenyl)- butanol-1 (III)	148—149 (6)	1.5243	1.0237	61.60	61.33	75.66	8.88	$C_{13}H_{18}O_2$	75.73	8.74	201.2	206	74.6
2-Methyl-1-(o-allyloxy- phenyl)-propanol-1 (IV)	144—146 (5)	1.5262	1.0378	60.94	61.33	75.31	8.55	$C_{13}H_{18}O_2$	75.73	8.74	195.7	206	58.8
1-(o-Allyloxyphenyl)- pentanol-1 (V)	169—171 (7)	1.5199	1.0070	66.60	65.95	76.02	8.96	$C_{14}H_{20}O_2$	76.36	9.09	214.1	220	80.0
4-Methyl-1-(o-allyloxy- phenyl)-pentanol-1 (VI)	157—158 (3)	1.5136	0.9883	71.24	70.57	77.32	9.68	$C_{15}H_{22}O_2$	76.92	9.40	233.7	234	70.5
2-Methyl-1-(o-allyloxy- phenyl)-octanol-1 (VII)	178—180 (3)	1.5079	0.9695	84.86	84.42	78.40	9.91	$C_{18}H_{28}O_2$	78.22	10.14	276.6	276	56.7

SUMMARY

1. The reaction of an allyl ester of salicylic aldehyde with several alkylmagnesium halides has been carried out.

2. Seven alkyl-(o-allyloxyphenyl)-carbinols were prepared, which are not described in the literature.

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INVESTIGATIONS ON THE TRANSFORMATION OF PINACOLS
CONTAINING ACETYLENIC RADICALS AS SUBSTITUENTS
XIX. THE INTERACTION OF DIMETHYLBENZOYL CARBINOL WITH
VINYLACETYLENE IN LIQUID AMMONIA IN THE PRESENCE
OF SODAMIDE

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We recently found [1] that in the reaction of vinylacetylene with diphenylacetylcarbinol in liquid ammonia in the presence of sodamide, the product was not the expected glycol of the vinylacetylene series, namely asym-methyldiphenyl(vinylethynyl)ethanediol (2-methyl-1,1-diphenylhexa-5-en-3-yne-1,2-diol), but a dienol alcohol with an acetylenic terminal group, namely 1,1-diphenyl-2-methylenhexa-3-en-5-yne-1-ol.

The formation of this alcohol was attributed to a double prototropic regrouping of the normal synthesis product - asym-methyldiphenyl(vinylethynyl)ethanediol - via an intermediate triene, followed by dehydration of the resulting isomeric diol containing an unsubstituted acetylenic terminal group.

It was also found that asym-methyldiphenyl(vinylethynyl)ethanediol split up under the influence of sodamide to form benzophenone and, evidently, hexa-1,3-dien-5-yne resulting from dehydration of hexa-3-en-5-yne-2-ol.

Synthesis of asym-dimethylphenyl- and asym-methyldiphenyl(vinylethynyl)ethanediols by the Iotsich method proceeded normally [1, 2].

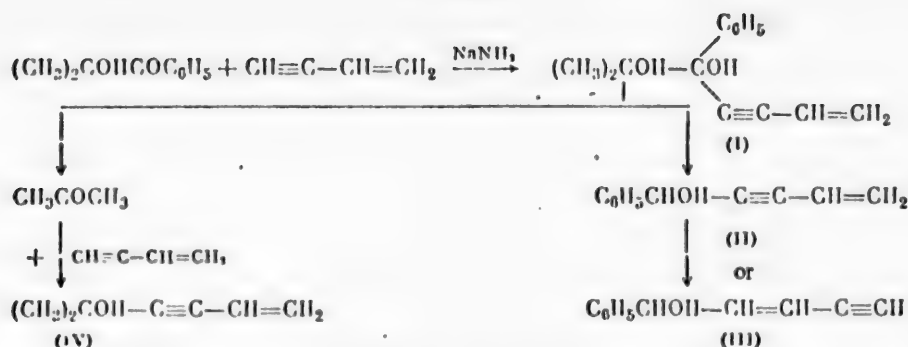
In view of the above it was of interest to find out whether the formation of asym-dimethylphenyl(vinylethynyl)ethanediol proceeded normally under the conditions of ammoniacal synthesis [3], or whether there were deviations from the normal course of reaction in the case of this diol.

The result obtained was quite unexpected, for the product from the interaction of dimethylbenzoylcarbinol with vinylacetylene in the presence of sodamide was dimethylvinylethynylcarbinol (IV). This product was obtained in good yield and was identified by analysis, physical constants, infrared spectrum, splitting with potash [4], oxidation to acetone, formic acid, and oxalic acid, and reduction to dimethylbutylcarbinol. The isomeric alcohol with an unsubstituted acetylenic end group $-(CH_3)_2COH-CH=CH-C\equiv CH$ [5] - was not detected.

In addition to the dimethylvinylethynylcarbinol there was an appreciable amount of oily residue, which quickly set to a glassy mass, but only in one experiment was it possible to isolate a small amount of a liquid boiling at a considerably higher temperature than the carbinol. There was too little of this liquid for a thorough investigation. The analytical data corresponded to the formula $C_{11}H_{10}O$, indicating that the liquid might be a secondary product of ketonic splitting of the diol, namely 1-phenylpenta-4-en-2-yne-1-ol (II) or its isomerization product 1-phenylpenta-2-en-4-yne-1-ol (III). However, the infrared spectrum did not show the presence of an unsubstituted acetylenic end group, so that the structure of this liquid remained undetermined.

The interaction of dimethylbenzoylcarbinol with vinylacetylene in the presence of sodamide can be represented as follows:

Scheme



Asym-dimethylphenyl(vinylethynyl)ethanediol (I), obtained from dimethylbenzoylcarbinol and vinylacetylene, breaks down by ketonic splitting into acetone and the alcohol (II), which can isomerize to the alcohol (III). Under the synthesis conditions, acetone condenses with excess vinylacetylene to give dimethylvinylethynylcarbinol (IV), while the alcohols (II or III) are converted into polymers.

There is a statement in the literature that the alcohol (II) rapidly turns yellow and that a considerable amount of red glassy resin is formed on vacuum distillation [6].

It might be supposed that the acetone is not formed by ketonic splitting of the vinylethynyl diol (I) but by decomposition of dimethylbenzoylcarbinol under the influence of sodamide to give acetone and benzaldehyde; the latter could then react with vinylacetylene to give the corresponding alcohol. A special experiment on the action of sodamide in liquid ammonia on dimethylbenzoylcarbinol gave negative results; the carbinol was recovered unchanged.

EXPERIMENTAL

1. Interaction of Dimethylbenzoylcarbinol with Vinylacetylene in the Presence of Sodamide

A little $\text{Fe}(\text{NO}_3)_3$ was added to 800 ml of liquid ammonia, 9 g of metallic sodium was added in small pieces during 30 min, and 50 ml of vinylacetylene (approximately 5.5 times the theoretical quantity for the amount of dimethylbenzoylcarbinol to be used) was passed in. The reaction mixture was then stirred for 30 min. Then 20 g of the ketoalcohol (b. p. 117° at 5 mm) in solution in anhydrous ether was added drop by drop. The next day the reaction mixture was decomposed with cold water and very dilute sulfuric acid, the ether layer was separated, and the aqueous layer was extracted with ether; the ether layer and extract were combined, washed with soda and then with water, and dried over sodium sulfate. The ether was distilled off to leave a thick dark liquid; vacuum distillation of this gave two fractions - the first of 5.7 g boiling at 55° (2 mm) and the second of 2.17 g boiling at $110-120^\circ$ (2 mm). There was about 40% of tarry residue.

In a repeat experiment, using 40 g of dimethylbenzoylcarbinol, 17 g of sodium and a fourfold excess of vinylacetylene, there was only one product corresponding to the first fraction with a b. p. of 37° (1 mm). This was a colorless mobile liquid which polymerized on standing to a glassy material insoluble in benzene.

2. Investigation of the First Fraction with a b. p. of 55° (2 mm)

This material had the following properties after repeated distillation: b. p. 37° (1 mm), d_{20}^{20} 0.8895, n_D^{20} 1.4758.

Found %: C 76.44, 76.58; H 9.30, 9.40; H_{act} , 0.99. No. of H_{act} , 1.22, 1.08. Mol. wt. 116.9. Calc. for $\text{C}_7\text{H}_{10}\text{O}$. Calculated %: C 76.36; H 9.09; H_{act} , 0.91. No. of H_{act} , 1. Mol. wt. 110.

The infrared spectrum showed the following absorption frequencies: ~ 3400 ($-\text{OH}$), 919, 942, 991 ($-\text{CH}=\text{CH}_2$), 2205 cm^{-1} ($-\text{C}\equiv\text{C}-$)².

*The infrared spectrum was recorded with an IKS-15 spectrophotometer, using LiF and NaCl prisms, over the range $700-3400\text{ cm}^{-1}$, with a slit width from 20-220 μ . Our thanks are due to T. V. Yakovleva for recording and interpreting the spectra.

The material gave a very slight turbidity with ammoniacal silver oxide, potassium permanganate was decolorized immediately, there was an evolution of gas with Grignard reagent, and 2,4-dinitrophenylhydrazine gave a negative reaction.

From the analytic data, the values of the constants, and the products obtained, the material was dimethylvinylethynylcarbinol.

The literature data for dimethylvinylethynylcarbinol is: b. p. 58–59° (13 mm); d_{15}^{15} 0.8925; n_D^{15} 1.4786 [7]; b. p. 53–54° (10 mm), n_D^{19} 1.4770 [8].

Oxidation of dimethylvinylethynylcarbinol. A 5.5 g sample (b. p. 37° at 1 mm) was oxidized with 19.8 g of potassium permanganate (10 g as 2% solution and 9.8 g in dry form). Decolorization was rapid; oxidation was not carried to completion, although further quantities of potassium permanganate added were still decolorized. Manganese dioxide was removed by distilling the strongly alkaline solution directly into a solution of 2,4-dinitrophenylhydrazine; the resulting hydrazone melted at 123–124°, and gave no m. p. depression when mixed with the 2,4-dinitrophenylhydrazone of acetone.

Found %: C 45.57; H 4.52; N 23.39, 23.48. Calc. for $C_9H_{10}O_4N_4$: Calculated %: C 45.38; H 4.23; N 23.48.

Formic acid was detected qualitatively in the acid volatile in steam, and oxalic acid (m. p. 100–101° for mixed sample) was found in the nonvolatile acid.

Hydrogenation of dimethylvinylethynylcarbinol. A 4.5647 g sample was hydrogenated in methanol solution in the presence of 0.7 g of Pd/CaCO₃. Over a period of 4 hr 29 min 3041 ml of hydrogen was absorbed (this compares with a theoretical 2916 ml at 19° and 771 mm, assuming 3 mole hydrogen per mole carbinol). The methanol was then distilled off up a column, and the hydrogenation product was redistilled in vacuo.

B. p. 63° (22 mm); d_{20}^{20} 0.8184; n_D^{20} 1.4174.

Found %: C 72.20, 72.36; H 13.92, 13.94; H_{act} , 0.95. No. of H_{act} , 1.09. M 113.6. $C_7H_{16}O$.

Calculated %: C 72.35; H 13.88; H_{act} 0.87. No. of H_{act} 1. Mol. wt. 116.

The product was therefore dimethylbutylcarbinol.

Literature data [9, 10] for the carbinol is: b. p. 139–140° (740 mm), n_D^{20} 1.4175; b. p. 58–60° (20 mm), d_{20}^{20} 0.815, n_D^{20} 1.4187.

3. Investigation of the Second Fraction with a b. p. of 110–120° (2 mm)

The material boiled at 120–124° (2 mm) after a second distillation (compare [6]).

Found %: C 83.12, 82.90; H 7.09, 7.75; H_{act} , 1.25. No. of H_{act} , 1.96. Mol. wt. 139.8. Calc. for $C_{11}H_{10}O$: Calculated %: C 83.54; H 6.33; H_{act} , 0.63. Mol. wt. 158. The No. of H_{act} is 1 for a unifunctional alcohol with a vinyl terminal group (II) (compare [6]), giving % H_{act} = 1.26. The No. of H_{act} is 2 for a unifunctional alcohol with an acetylenic terminal group (III).

The material rapidly became yellow and thick on standing. It partially decomposed on redistillation in vacuo, forming a considerable amount of dark residue which congealed rapidly.

The infrared spectrum was recorded with an IKS-14 spectrophotometer, using LiF and NaCl prisms, over the range 700–3400 cm^{-1} , with a slit width of 36 μ . Absorption bands were observed at the following frequencies: 3400, 2191, 1600, 998, 971, 919, and 703 cm^{-1} .

From these results it was not possible to say whether the product of b. p. 120–124° (2 mm) was the alcohol II or III.

Thus it was found that the reaction between dimethylbenzoylcarbinol and vinylacetylene gave dimethylvinylethynylcarbinol; the yield, based on the original dimethylbenzoylcarbinol, was 42.8% (experiment 1) and 78% (experiment 2). The unifunctional alcohol II or III was also formed in 11.3% yield (experiment 1).

SUMMARY

It has been shown that in the reaction between dimethylbenzoylcarbinol and vinylacetylene in liquid ammonia in the presence of sodamide, there is ketonic splitting of the primary product, namely asym-dimethylphenyl(vinylethynyl)ethanediol (2-methyl-3-phenylhepta-6-en-4-yne-2,3-diol).

The acetone formed under these conditions reacts with vinylacetylene to give a high yield of dimethylvinylethynylcarbinol.

Another part of the originally formed diol gives one of the isomeric unfunctional alcohols: 1-phenylpenta-4-en-2-yne-1-ol or 1-phenylpenta-2-en-4-yne-1-ol. The structure of the product has not been determined.

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HETEROCYCLIC COMPOUNDS

SYNTHESIS OF 2,5-DIMETHYL-4-ETHYNYL(VINYL AND ETHYL)

PIPERIDINE-4-OLS

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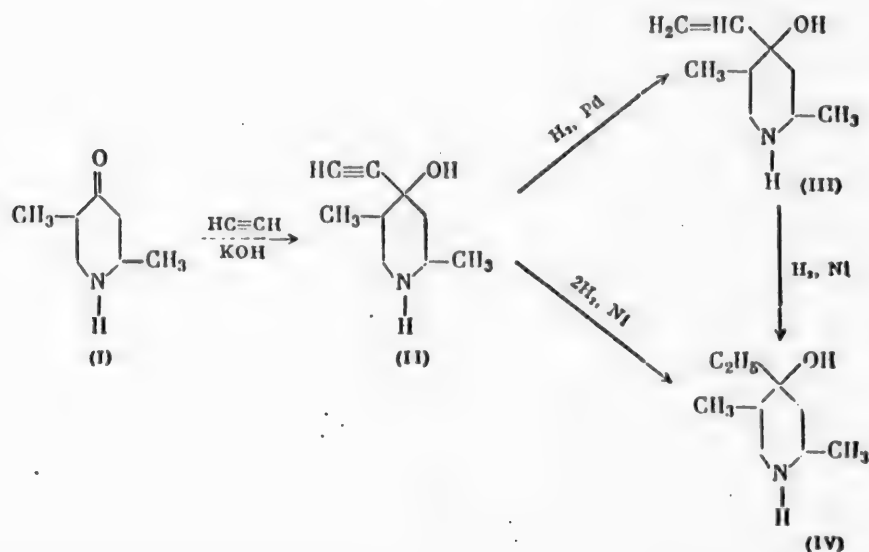
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In a previous paper [1] 2,5-dimethyl-4-ethynylpiperidine-4-ol (II) was described as a liquid which crystallized slowly. In the present paper we describe the separation of the mixture of stereoisomers of this piperidineol into three separate stereoisomers: γ -isomer of m. p. 93–94° (yield 42.5% of total mixture), β -isomer of m. p. 131–132° (14.2% yield), and a liquid isomer of b. p. 96–98° (2 mm) (2.41% yield). By selective hydrogenation over a palladium catalyst of the individual forms of the piperidineol (II) we obtained the three stereoisomers of 2,5-dimethyl-4-vinylpiperidine-4-ol (III): γ -isomer of m. p. 125–126° [1], β -isomer of m. p. 82–83°, and a liquid isomer of b. p. 93–95° (2 mm).

Exhaustive hydrogenation over a nickel catalyst of the individual stereoisomers of 2,5-dimethyl-4-ethynylpiperidine-4-ol (II) and of 2,5-dimethyl-4-vinylpiperidine-4-ol (III) gave the three stereoisomers of 2,5-dimethyl-4-ethylpiperidine-4-ol (IV): γ -isomer of m. p. 135–136° [1], β -isomer of m. p. 98–99°, and a liquid isomer of b. p. 90–92° (2 mm).

The 2,5-dimethyl-4-ethynylpiperidine-4-ol (II) [1] was obtained in high yield by the condensation of acetylene with dimethylpiperidone (I) [2] by the method of Favorskii and Nazarov [3–5].



EXPERIMENTAL

2,5-Dimethylpiperidine-4-one (I). A mixture of 125 g of propenyl isopropynyl ketone and of the corresponding β -methoxyketone, obtained by reacting it with methanol (n_D^{20} 1.4505) [6], with 800 ml of 25% ammonia in water was heated in a sealed vessel for 6 hr on a boiling water bath. The experiment was repeated and the products were combined. The ammonia was then distilled off in the vacuum from a water pump, first at room temperature and then at 60° on a water bath. The solution, which had been reduced to a volume of about a liter by evaporation, was acidified with cold concentrated hydrochloric acid until it gave an acid reaction with Congo Red. The acid solution was extracted with ether, then evaporated down to about 0.3 liters, cooled, and made alkaline with 50% caustic soda solution. The bases thrown out of solution were separated and dissolved in ether, and the alkaline aqueous layer was saturated with salt and carefully extracted with 15 portions of ether. The combined ether solution were dried over sodium sulfate. The ether was then distilled off, and the residue was distilled in vacuo to give 121 g of I [2, 7], b. p. 77–80° (5 mm), n_D^{20} 1.4668.

2,5-Dimethyl-4-ethynylpiperidine-4-ol (II). A three-neck flask was fitted with a stirrer, a reflux condenser, a dropping funnel, and a tube for passing in acetylene. To this were added 1570 ml of anhydrous ether, 140 g of powdered caustic potash, and 15 ml of anhydrous alcohol; the mixture was stirred vigorously and cooled to -3°, while being saturated with purified acetylene for 2 hr. Passage of a vigorous acetylene stream and stirring were continued while a solution of 159 g of 2,5-dimethylpiperidine-4-one (n_D^{20} 1.4667) [3] in 160 ml of anhydrous ether was added, drop by drop, over a period of 2.5 hr. The acetylene stream was then continued for a further 4 hr. All this time the temperature was maintained at 0 to -3°. The reaction product was hydrolyzed with 250 ml of water, keeping it cold. The ether layer was separated, and the alkaline aqueous layer was saturated with salt and extracted several times with ether. The combined ether solutions were treated with saturated salt solution. The ether solution was then dried with sodium sulfate, the ether was distilled off, and the residue was distilled in vacuo. The product was 167.4 g (87.5%) of the mixed stereoisomers of II in the form of a thick liquid, b. p. 114–118° (2 mm), n_D^{20} 1.5025 [1]. The residue in the distillation flask weighed 2 g.

A 510 g quantity of the mixed stereoisomers was dissolved in 600 ml of anhydrous benzene, and 350 ml of petroleum ether was added until the solution became turbid. The deposit, weighing 220.8 g, was filtered off, and a further 247.2 g of material was precipitated from the mother liquor by further addition of petroleum ether. Altogether 468 g (91.76%) of crystalline isomers of II was obtained, of m. p. 79–84°. Further fractional crystallization from benzene yielded the two separate crystalline isomers of II.

1) γ -Isomer, m. p. 93–94°, 217.3 g (42.5%).

Found %: N 9.08, 9.12. Calc. for $C_9H_{15}ON$: Calculated %: N 9.15.

The hydrochloride of the γ -isomer was obtained by mixing an ethereal solution with a dry ethereal solution of hydrochloric acid; it was recrystallized from absolute alcohol. The product from 3 g of II was 3.5 g (97%) of the hydrochloride, of m. p. 191–192°.

Found %: N 7.20, 7.39. Calc. for $C_9H_{16}ONCl$: Calculated %: N 7.38.

2) β -Isomer, m. p. 131–132°, 72.4 g (14.2%).

Found %: N 9.04, 9.15. Calc. for $C_9H_{15}ON$: Calculated %: N 9.15.

The hydrochloride of the β -isomer melted at 234–235° (from alcohol). One g of II gave 0.9 g of hydrochloride.

Found %: Cl 18.64, 18.51. Calc. for $C_9H_{16}ONCl$: Calculated %: Cl 18.69.

A mixture of γ - and β -isomers gave a lower melting point.

The solvent (benzene and petroleum ether) was distilled off from the mother liquor after deposition of the crystalline isomers, and the residue was distilled in vacuo. The product was 12.3 g (2.41%) of the liquid isomer of II.

B. p. 96–98° (2 mm); n_D^{20} 1.4905; d_4^{20} 0.9934; MR_D 44.56, calc. 44.68.

Found %: N 9.08, 9.12. Calc. for $C_9H_{15}ON$: Calculated %: N 9.15.

The hydrochloride of the liquid isomer remained liquid and did not crystallize.

After the above mentioned quantities of the individual isomers of II had been isolated, there remained 95.5 g of a crystalline mixture of m. p. 70–100°, and 85 g of a thick liquid with n_D^{20} 1.5030.

2,5-Dimethyl-4-vinylpiperidine-4-ol (III). a) The flask for hydrogenation of organic compounds was fitted with a mechanical shaker. Into this were placed 0.07 g of Pd/CaCO₃ catalyst, prepared by the method of Busch and Stöve [8], and 20 ml of absolute alcohol, and the catalyst was saturated with dry hydrogen for an hour. Then 6.02 g of the γ -isomer of II (m. p. 93–94°) was introduced in 80 ml of absolute alcohol, the air was displaced by hydrogen, and the material was hydrogenated under normal conditions (20° and 694.4 mm) for 39 min, until 1035 ml of hydrogen had been absorbed; this was the volume calculated for the reduction of one bond in the weight of II taken. The catalyst was filtered off and washed, the alcohol was distilled off, and the residue was found to be crystalline. Recrystallization from benzene gave 5.95 g of the γ -isomer of III of m. p. 125–126° [1].

Found %: N 9.15, 8.85. Calc. for C₉H₁₇ON: Calculated %: N 9.02.

The hydrochloride of the III γ -isomer was obtained by mixing an alcoholic solution with a dry ethereal solution of hydrochloric acid and precipitating with ether. From 0.4 g of III the yield was 0.3 g of hydrochloride, of m. p. 199–200° (from alcohol).

Found %: Cl 18.33, 18.36. Calc. for C₉H₁₈ONCl: Calculated %: Cl 18.50.

b) A 9 g sample of the II β -isomer (m. p. 131–132°), dissolved in 100 ml of absolute alcohol, was subjected to selective hydrogenation in the presence of 0.1 g of Pd/CaCO₃ catalyst at 17° and 693.7 mm. After 55 min, 1529 ml of hydrogen, the calculated volume for saturating one bond in the sample taken, had been absorbed and the hydrogenation was stopped. The catalyst was filtered off, the alcohol was distilled off, and the residue was recrystallized from benzene. The product was 8.83 g of the β -isomer of III of m. p. 82–83°.

Found %: N 8.95, 8.86. Calc. for C₉H₁₇ON: Calculated %: N 9.02.

The hydrochloride of the β -isomer, recrystallized from a mixture of alcohol and ether, melted at 182–183° (from a mixture of alcohol and ether). The yield from 0.4 g of base was 0.37 g of hydrochloride.

Found %: N 7.32, 7.25; Cl 18.76, 18.95. Calc. for C₉H₁₈ONCl: Calculated %: N 7.31; Cl 18.50.

c) A 76.6 g sample of the unresolved mixed stereoisomers of II, in the form of a thick liquid (n_D^{20} 1.5025), was dissolved in 275 ml of absolute alcohol and reduced in the presence of 1 g of Pd/CaCO₃ catalyst, at 14° and 696 mm, for 1.5 hr, until 12.85 liters of hydrogen had been absorbed, this being the calculated quantity for the reduction of one bond in the sample of II. The catalyst was filtered off, the alcohol was distilled off, and the residue was subjected to fractional crystallization from benzene. The products were 34.76 g (45.5%) of the γ -isomer of III of m. p. 125–126°, and 6.37 g (8.32%) of the β -isomer, of m. p. 82–83°.

The residue, after the removal of these individual forms of III, was 20.16 g (26.31%) of an unresolved crystalline mixture of stereoisomers of m. p. 55–70°.

The benzene was distilled off from the mother liquor, and the residue was distilled in vacuo to give 13 g (17%) of the III liquid isomer.

B. p. 93–95° (2 mm); n_D^{20} 1.4930; d_4^{20} 0.9833; MR_D 45.82, calc. 46.22.

Found %: N 8.92, 9.05. Calc. for C₉H₁₇ON: Calculated %: N 9.02.

2,5-Dimethyl-4-ethylpiperidine-4-ol (IV). a) A 3.06 g sample of the γ -isomer of II (m. p. 93–94°), dissolved in 30 ml of absolute alcohol, was subjected to exhaustive hydrogenation at 22° and 694 mm over 1.25 g of Raney nickel catalyst. The hydrogen absorbed was 887 ml (corrected to N. T. P.). The catalyst was filtered off and washed, the alcohol was distilled off, and the residue was twice recrystallized from benzene. The product was 2.7 g (87%) of the γ -isomer of IV, of m. p. 135–136° [1].

Found %: N 8.87, 8.93. Calc. for C₉H₁₉ON: Calculated %: N 8.91.

The hydrochloride of the IV γ -isomer had an m. p. of 211–212° (from a mixture of alcohol and ether). The yield was 0.22 g of hydrochloride from 0.2 g of base.

Found %: Cl 18.31, 18.08. Calc. for $C_9H_{20}ONCl$: Calculated %: Cl 18.30.

b) An 11 g sample of the β -isomer of II (m. p. 131–132°), dissolved in 75 ml of absolute alcohol, was hydrogenated at 20° and 698.7 mm, in the presence of 3.6 g of Raney nickel, until no more hydrogen was absorbed; the total volume absorbed was 3 liters. The catalyst was filtered off, the alcohol was distilled off, and the product was recrystallized from benzene. The yield was 10.2 g (90.3%) of the β -isomer of IV, of m. p. 98–99°.

Found %: N 8.88, 9.10. Calc. for $C_9H_{19}ON$: Calculated %: N 8.91.

The hydrochloride of the IV β -isomer melted at 172–173° (from alcohol).

Found %: Cl 18.31, 18.32. Calc. for $C_9H_{20}ONCl$: Calculated %: Cl 18.30.

c) A 4.6 g sample of the liquid isomer of II (n_D^{20} 1.4905), dissolved in 30 ml of absolute alcohol, was subjected to exhaustive hydrogenation at 16° and 697.5 mm, over 2.4 g of Raney nickel, until the calculated volume of hydrogen (1344 ml at N. T. P.) had been absorbed. The catalyst was filtered off, the alcohol distilled off, and the residue redistilled in vacuo to give 4.2 g (89%) of the liquid isomer of IV.

B. p. 90–92° (2 mm), n_D^{20} 1.4865, d_4^{20} 0.9693, MR_D 46.55, calc. 46.69.

Found %: N 8.92, 8.79. Calc. for $C_9H_{19}ON$: Calculated %: N 8.91.

The hydrochloride of the IV liquid isomer was a liquid which would not crystallize.

d) A 20 g sample of mixed stereoisomers of II (n_D^{20} 1.5030), in the form of the liquid after separation of some of the crystalline isomers, dissolved in 40 ml of absolute alcohol, was subjected to hydrogenation at 19° and 697.2 mm, over 7.0 g of Raney nickel, until 5.80 liters of hydrogen (corrected to N. T. P.) had been absorbed. The catalyst was filtered off and the alcohol distilled off. The residue was recrystallized twice from benzene to give 13 g (63.4%) of the IV γ -isomer, of m. p. 135–136°.

The benzene was distilled off from the mother liquor, and the residue was redistilled in vacuo to give 4.9 g (– 25%) of the IV liquid isomer.

B. p. 91–92° (2 mm); n_D^{20} 1.4850; d_4^{20} 0.9716; MR_D 46.51, calc. 46.69.

e) A 4.65 g sample of the γ -isomer of III (m. p. 125–126°), dissolved in 50 ml of absolute alcohol, was hydrogenated over 1 g of Raney nickel until 788 ml of hydrogen had been absorbed (18° and 697 mm). The catalyst was filtered off, the alcohol was distilled off, and the residue was recrystallized from benzene. The product was 4.5 g of the γ -isomer of IV, of m. p. 135–136° [1].

f) A 1.7 g sample of the β -isomer of III (m. p. 82–83°), dissolved in 25 ml of absolute alcohol, was hydrogenated in the presence of 1 g of Raney nickel, under the normal conditions for complete reduction; the volume of hydrogen absorbed was 285 ml. The product was recrystallized from benzene to give 1.6 g of the IV β -isomer, of m. p. 98–99°.

g) A 4.65 g sample of the liquid isomer of III (b. p. 93–95° at 2 mm, n_D^{20} 1.4930), dissolved in 50 ml of absolute alcohol, was hydrogenated over 2 g of Raney nickel until the calculated quantity of hydrogen (772 ml at 11° and 700 mm) had been absorbed. The catalyst was filtered off, the alcohol distilled off, and the residue redistilled in vacuo. The product was 4 g of the IV liquid isomer.

B. p. 91–93° (2 mm), n_D^{20} 1.4860, d_4^{20} 0.9586, MR_D 46.46, calc. 46.69.

SUMMARY

1. A mixture of stereoisomers of 2,5-dimethyl-4-ethynylpiperidine-4-ol has been resolved to give two separate crystalline isomers and one liquid isomer.

2. Partial hydrogenation of the individual isomers of 2,5-dimethyl-4-ethynylpiperidine-4-ol gave two crystalline and one liquid isomer of 2,5-dimethyl-4-vinylpiperidine-4-ol (one has been described earlier). Exhaustive hydrogenation of the individual isomers of 2,5-dimethyl-4-ethynylpiperidine-4-ol, or of 2,5-dimethyl-4-vinylpiperidine-4-ol, gave two crystalline and one liquid isomer of 2,5-dimethyl-4-ethylpiperidine-4-ol (one has been described earlier).

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THE CHARACTERISTICS OF DITERTIARY β -GLYCOLS. I

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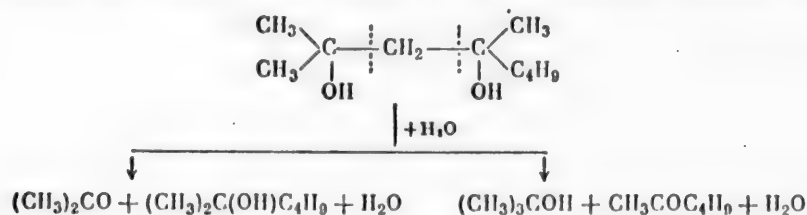
Original article submitted August 18, 1959

Ditertiary β -glycols have been obtained by complete synthesis by the action on RMgX of malonic [1], dimethylmalonic [2], ethylacetoacetic [3], and dimethylacetoacetic [4] esters. Worse results were obtained with β -diketones [5]. Most of the known ditertiary β -glycols have been obtained by the action of tertiary β -ketols on AlkMgX [6] or ArMgX [7]. According to our results, the latter reaction for partial synthesis is quite satisfactory provided that three conditions are observed: the initial β -ketol must have been freshly redistilled, the primary Grignard reaction product must be decomposed with water without local overheating, and the end product from the Grignard reaction must be absolutely neutral before vacuum distillation.

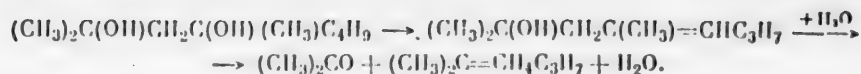
Kalishev [2] and Slavyanov [2] were the first to observe the splitting up of hexamethyltrimethylene glycol on boiling with dilute acids. Kalishev interpreted this process as a dehydration of the β -glycol to a β -oxide, followed by fission to acetone and tetramethylethylene. Slavyanov was close to a true understanding of the nature of this reaction; in his scheme water took part in the splitting of the β -glycol to acetone and dimethylisopropylcarbinol, and the latter was then dehydrated to tetramethylethylene. However, Slavyanov [4] also pointed out that his glycol "was extremely easily dehydrated with fission to hexene and acetone."

It has been recorded in the literature [8] that the action of sulfuric acid, under different conditions, on 2,4-dimethylpenta-2,4-diol gives a fraction of b. p. 59-80°, but this fraction was not further investigated because the main interest was in the isolation of the product of partial dehydration of the glycol, namely 2,4-dimethylpenta-4-en-2-ol. It has also been recorded that β -ditertiary glycols are very easily dehydrated to give dienic hydrocarbons [6].

Our investigations on the hydrolytic splitting of five ditertiary β -glycols showed that, as a result of the hydrolytic splitting of their molecules occurring in an alkaline medium and very much more so in an acid medium, they all gave a positive iodoform reaction (see table). This may be explained as due to a direct hydrolytic splitting of one or both of the C-C bonds between the carbinol C atoms and the C atom separating them, to give a mixture of methyl ketones and of tertiary alcohols, or of the alkene dehydration products of the latter.



However, we cannot exclude a second interpretation based on the facts that ditertiary β -glycols can be converted into β - γ -unsaturated tertiary alcohols [8], and that the latter, as shown by Favorskaya and Fridman [9] for alkylaryl- and diarylallylcarbinols and by Esafov [10] for dialkylallylcarbinols, are capable of undergoing ketonic splitting. One of the possible routes for the dehydration of a β -glycol is shown below.



If the second mechanism is assumed to be correct (it must be definitely excluded for the case of hexamethyltrimethyleneglycol), then it is only logical to suppose that the β - γ -unsaturated alcohol must undergo hydrolytic splitting more easily than the ditertiary β -glycol. In order to test this point, experiments were carried out on the hydrolytic splitting of methylethylallylcarbinol. These showed that the carbinol split up with considerably more difficulty than the one of the five β -glycols investigated which was most similar to it in structure, namely 2,4-dimethylhexa-2,4-diol (see table, experiments 16-18).

In order to confirm this indirect evidence, a sample of 2,4-dimethylocta-2,4-diol was distilled in the presence of 0.1 N sulfuric acid. Acetone, 2-methylhexa-2-ene, methyl butyl ketone, and, qualitatively, trimethyl- and dimethylbutyl-carbinols were found in the fission products. On this basis it follows that ditertiary β -glycols are subject to hydrolytic splitting on heating in an alkaline medium, or still more so in an acid medium. Consequently, substances containing a ditertiary β -glycol grouping must be added to the list of known organic compounds capable of undergoing hydrolytic fission at the C-C bond.

EXPERIMENTAL

The ditertiary β -glycols were synthesized* in the apparatus described previously [11]. In all the preparations a solution of 0.25 mole of diacetonyl alcohol (d_4^{20} 0.9501; n_D^{20} 1.4217; M_R^D 31.44) in anhydrous ether (1 : 1) was added to 0.5 mole of RMgX at 18-20° over a period of 3 hr. The reaction mixture was allowed to stand for 12 hr, then cooled in ice and salt and cautiously decomposed with 50 ml of ice water while stirring continuously. The ether layer was separated, and the viscous residue was dissolved in dilute (1 : 3) acetic acid, saturated with salt, and extracted three times with ether. The combined ether solutions were washed with dilute soda solution and then with water till neutral, and dried over anhydrous sodium sulfate. The liquid was then filtered, the ether distilled off, and the residue was distilled first at 100 mm to remove volatile components and then at 1.5-5 mm. Acetone was present among the low boiling components in all the syntheses, and there was a 5% yield of dimethylbutylcarbinol in the synthesis from $\text{C}_4\text{H}_9\text{MgBr}$. There was 7.4% by volume of ethylene in the gas obtained from the synthesis with $\text{C}_2\text{H}_5\text{MgBr}$. In the syntheses from α -naphthylmagnesium bromide, the product from the Grignard reaction was treated with water vapor, after distilling off the ether, in order to remove naphthalene. 2-Methyl-4- α -naphthylpenta-2,4-diol was recrystallized from ligroin and finally from a mixture of alcohol and petroleum ether; its m. p. was 125° [7]. The other β -glycols had constants agreeing with literature data [6-8]. In the case of syntheses from methylmagnesium iodide and butylmagnesium bromide, using diacetonyl alcohol (n_D^{20} 1.4192) which had not been freshly distilled but had been stored for a year sealed in ordinary glass phials exposed to diffuse light, the yields of 2,4-dimethylpenta-2,4-diol and 2,4-dimethylocta-2,4-diol were 18 and 15%. Using freshly distilled diacetonyl alcohol and methylmagnesium iodide, ethyl-, butyl-, phenyl-, and naphthyl-magnesium bromides, the yields were 61, 46, 58, 32, and 30%.

In experiments to determine the degree of hydrolytic splitting of the β -glycols and of methylethylallylcarbinol (b. p. 138.5-139° at 739 mm; d_4^{20} 0.8324; n_D^{20} 1.4308; M_R^D 35.49), approximately 0.001 mole samples were sealed up with either 10 ml of 0.1 N KOH (experiments 1, 4, 7, and 16 in table), or 10 ml of N KOH (experiments 2, 5, 8, 10, 13, and 17), or 10 ml of dioxane* + 10 ml of N KOH (experiments 11 and 14), or 10 ml of 0.1 N H_2SO_4 (experiments 3, 6, 9, 12, 15, and 18), and the ampules were heated in a boiling water bath for 2 hr. In the experiments with KOH solution, the contents of the cooled ampules were then transferred to flasks, treated with 25 ml of 0.1 N aqueous iodine and 25 ml of N NaOH, and allowed to stand for 15 min. Enough N hydrochloric acid was added to give 1 ml excess, and the unreacted iodine was titrated with 0.1 N thiosulfate solution. In the experiments with sulfuric acid solution, the contents of the ampules were transferred to 100 ml graduated flasks and made up to the mark. Aliquot portions of 10 ml were taken to investigate the iodoform reaction; the solutions were not filtered in experiments 3 and 6, but were filtered in experiments 9, 12, 15, and 18. Calculations of the degree of hydrolytic splitting were based on a consumption of 3 moles of iodine per mole of glycol or carbinol for 100% decomposition (see table).

* Syntheses were carried out by the students T. I. Osipova, N. M. Birlintseva, L. A. Samarina, F. A. Khasina, L. M. Romanova, M. V. Chupina, and T. I. Morozova.

* Dioxane was added to give a homogeneous solution.

TABLE

Expt. No.	Substance	Sample wt., g	Vol. of 0.1 N Na ₂ S ₂ O ₃ , ml*		Degree of hydrolytic splitting, % theoretical
			for titration of excess iodine	equiv. of iodine consumed	
1	2,4-Dimethylpenta-2,4-diol	0.1317	5.80	19.00	37.47
2		0.1353	4.73	20.07	32.67
3		0.1340	—	59.20	97.34
4	2,4-Dimethylhexa-2,4-diol	0.1507	8.32	16.48	26.66
5		0.1746	5.58	19.22	26.82
6		0.1251	—	48.06	93.63
7	2,4-Dimethylocta-2,4-diol	0.1723	23.0	1.80	3.03
8		0.1741	22.4	2.49	4.01
9		0.1785	—	40.50	65.89
10	2-Methyl-4-phenyl-penta-2,4-diol	0.1946	24.46	0.34	0.56
11		0.1947	23.66	1.14	1.89
12		0.1948	—	55.45	92.16
13	2-Methyl-4- α -naphthylpenta-2,4-diol	0.2436	24.56	0.24	0.40
14		0.2436	23.86	0.94	1.57
15		0.2440	10.64	14.16	23.63
16	Methylethylallyl-carbinol	0.1216	23.17	1.63	2.55
17		0.1322	22.97	1.83	2.63
18		0.1073	21.30	3.50	6.20

The results in the table show that all the ditertiary β -glycols gave positive iodoform reactions. The iodoform produced (experiments 3 and 9) melted at 118–119° after filtration, washing with water, drying, and recrystallization.

A 36 g sample of 2,4-dimethylocta-2,4-diol (b. p. 100.5° at 1.5 mm; d_4^{20} 0.9026; n_D^{20} 1.4440; MR_D 51.29) was redistilled in 3 g portions from a Claisen flask containing 50 ml of 0.1 N sulfuric acid; 30 ml of distillate were collected per hour, and 5 ml of water was added to the flask after each 5 ml of distillate had been collected. The yellowish sulfuric acid solution, containing a small amount of tarry material, was replaced by fresh acid after the distillation of every 6 g of β -glycol. The oily layers from the distillates were separated and heated to 148° on a metal bath to isolate the more volatile components; the residues were then subjected to a second distillation under the above stated conditions. The final products were 700 ml of aqueous liquid and 5.8 g of oil boiling up to 148°. The aqueous liquid yielded 0.8 g of material boiling at 57–59° (743 mm), which gave 0.9 g of a semicarbazone of m. p. 189°; this showed that acetone was present. A further 0.8 g of material from the aqueous liquid and 2.6 g from the oil, boiling in the range 60–100°, were extracted with water until there was no further volume change. The aqueous extract was filtered, and the filtrate was saturated with potash; 2 ml of a liquid was thus salted out; this gave a positive iodoform reaction and a Deniges reaction [12], and was identical with pure trimethylcarbinol.

The water-insoluble residue from the above 60–100° fraction was heated with metallic sodium at 80° and redistilled to give 1.2 g of 2-methylhexa-2-ene.

B. p. 91–92° (741 mm); d_4^{20} 0.7070; n_D^{20} 1.4020; MR_D 33.81, calc. for C₇H₁₄F 34.05; iodine No. 255.40 (Ganus), calc. 258.56.

The 2.7 g of the oil which boiled at 120–146° was shaken vigorously with a solution of 2.2 g of semicarbazide hydrochloride and 2.7 g of sodium acetate in 10 ml of water. Heat was evolved and a semicarbazone was formed. This semicarbazone was freed from oily impurities by shaking it several times with 1 : 2 alcohol

* In a blank experiment the consumption of 0.1 N Na₂S₂O₃ was 24.8 ml.

water mixture. The resulting 1.8 g of semicarbazone melted at 118°, confirming the presence of methyl butyl ketone [13]. The aqueous liquid decanted off from the semicarbazone and the aqueous alcohol washings were combined and treated with potash. The liquid salted out was dried over ignited potash, filtered and distilled. The residue from the alcohol distilled off showed a positive Deniges reaction.

SUMMARY

1. Conditions have been established for the synthesis of ditertiary β -glycols from tertiary β -ketols.
2. It has been found that ditertiary β -glycols have the general property that the bonds between one or both of the carbinol carbon atoms and the carbon atom separating them can be split by hydrolysis in an alkaline medium, and even more readily in an acid medium.

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THE CHEMISTRY OF UNSATURATED ETHERS

V. ACETALS OF VINYLACETALDEHYDE. NEW METHODS

OF OBTAINING 1-ALKOXY-1,3-DIENES*

S. M. Makin and B. K. Krupitsov

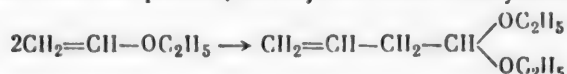
The Moscow Institute for Fine Chemical Technology

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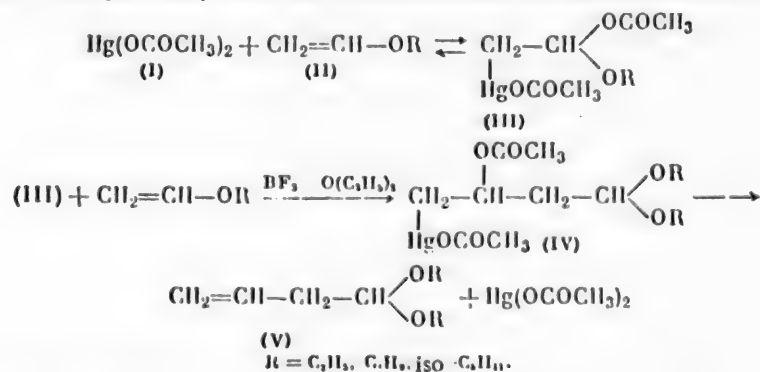
Original article submitted December 7, 1959

It is well known that vinyl alkyl ethers polymerize readily in the presence of acid reagents (FeCl_3 , BF_3 , etc) to give liquid and solid polymers [1]. However, as is stated in one of the patents [2], vinyl ethers can also undergo an autocondensation reaction in the presence of such complex catalysts as $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2 + \text{Hg}(\text{OCOCH}_3)_2$ or $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2 + \text{HgO}$, to give a dimerized product, namely the acetal of vinylacetaldehyde:



When we were completing the experimental part of our work, a paper was published on the autocondensation of vinyl ethers in the presence of the complex catalyst $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2 + \text{Hg}(\text{OCOCH}_3)_2$ [3].

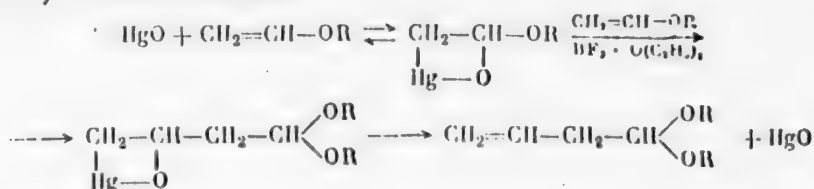
We investigated the autocondensation reactions of vinyl ethyl, vinyl butyl, and vinyl isoamyl ethers in the presence of $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$ complexed with HgO , $\text{Hg}(\text{OCOCH}_3)_2$, HgSO_4 , and HgCl_2 , of FeCl_3 complexed with HgO and $\text{Hg}(\text{OCOCH}_3)_2$, and of ZnCl_2 complexed with HgO . Acetone, dimethylformamide, diethyl ether, nitromethane, and acetophenone were used as solvents. It was found that the autocondensation reaction proceeded most readily in acetone or diethyl ether, using a catalyst consisting of $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$ complexed with HgO or $\text{Hg}(\text{OCOCH}_3)_2$. Under these conditions, there was a yield of up to 80% of the acetal of vinylacetaldehyde together with a small amount of the condensation products of the acetal with the vinyl alkyl ether. Special experiments showed that mercuric oxide and mercuric acetate were unable to bring about any autocondensation of vinyl ethers in the absence of the etherate of boron trifluoride. On the other hand, it is known that vinyl alkyl ethers polymerize readily in the presence of boron trifluoride etherate; it is most probable, therefore, that the autocondensation of vinyl alkyl ethers occurs in two stages. In the first stage, mercuric acetate combines with the vinyl alkyl ether at the double bond to give a mixed acetate-acyl derivative (III) [4], and, in the second stage, this combines with another molecule of vinyl alkyl ether under the influence of the boron trifluoride etherate, the reaction being similar to that previously described for the addition of acetals and ketals to a vinyl ether [5-7]:



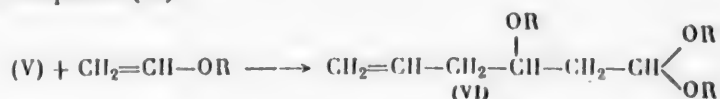
R = C₂H₅, C₄H₉, iso-C₅H₁₁.

* Part IV this journal 29, 3692 (1959).

The autocondensation of vinyl alkyl ethers in the presence of the complex catalyst $\text{HgO} + \text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$ can evidently occur by a similar mechanism:



Acetals of vinylacetaldehyde formed in this way can combine with another molecule of vinyl alkyl ether to give 1,1,3-trialkoxo compounds (VI):



However, this last reaction is slower, and the yield of VI is very small. In special experiments on the combination of vinylacetaldehyde diacetal with vinyl ethyl ether, the yield of 1,1,3-triethoxyhexa-5-ene (VI, $\text{R} = \text{C}_2\text{H}_5$) was only 24%.

In order to demonstrate that acetals of vinylacetaldehyde really were formed by the autocondensation of vinyl alkyl ethers, we recorded the infrared spectra of the autocondensation products from vinyl ethyl and vinyl butyl ethers and compared these with the spectrum of the diethylacetal of crotonaldehyde (made by acetalizing crotonaldehyde [8]).

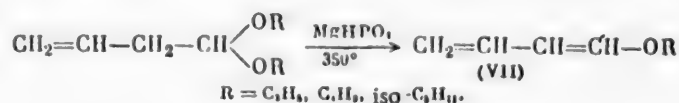
Examination of the absorption curves showed that the autocondensation product from vinyl ethyl ether gave bands at 3077 and 3016 cm^{-1} (weak), while the product from vinyl butyl ether gave a band at 3079 cm^{-1} . These bands are characteristic of the terminal vinyl grouping ($\text{CH}_2=\text{CH}-$) [9].

The diethylacetal of crotonaldehyde differed in having an absorption band at 3035 cm^{-1} , characteristic of the substituted vinyl grouping ($-\text{CH}=\text{CH}-$) [9].

Hydrogenation of the diethylacetal of vinylacetaldehyde (V , $\text{R} = \text{C}_2\text{H}_5$) gave the diethylacetal of butyric acid.

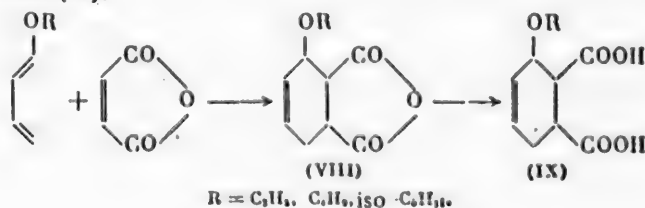
Hydrolysis of the acetal of vinylacetaldehyde by 5% phosphoric acid gave crotonaldehyde, i. e. the reaction was accompanied by allylic regrouping of the double bond to the α, β -position with respect to the carbonyl group. The action of 2,4-dinitrophenylhydrazine on the acetal of vinylacetaldehyde in an acid medium also gave the 2,4-dinitrophenylhydrazone of crotonaldehyde.

Since the vinylacetaldehyde acetals were readily obtained in good yield, it was of interest to investigate the possibility of obtaining alkoxydienes from them. It was found that passage of the acetal over an acid catalyst, under reduced pressure, at 350°, gave a good yield of the 1-alkoxybuta-1,3-diene (VII):



Thus the catalytic decomposition of acetals of vinylacetaldehyde provides a new and convenient method of obtaining 1-alkoxydienes.

Our 1-alkoxy-1,3-dienes gave adducts (VIII) with maleic anhydride, which hydrolyzed to give crystalline alkoxytetrahydrophthalic acids (IX):



EXPERIMENTAL

The diethylacetal of vinylacetaldehyde (V, R = C₂H₅). A mixture of 30 ml of acetone, 1 g of mercuric oxide, and 0.1 ml of boron trifluoride etherate was treated with 100 g of vinyl ethyl ether, added drop by drop, at 0°, during 2 hr, with vigorous stirring. The reaction mixture was stirred for a further 2 hr at 20°, neutralized with solid potash while continuing the stirring, filtered, and redistilled in vacuo. The product was 78.1 g (78.1%) of the diethylacetal of vinylacetaldehyde.

B. p. 70° (56 mm); n_D^{20} 1.4073; d_4^{20} 0.8450; MR_D 42.04, calc. 41.96.

Found %: C 66.90, 66.97; H 11.07, 11.27. Calc. for C₈H₁₆O₂: Calculated %: C 66.62; H 11.18.

The corresponding 2,4-dinitrophenylhydrazone was obtained by mixing an alcoholic solution of the acetal with an alcoholic solution of 2,4-dinitrophenylhydrazine sulfate [11]. The product was recrystallized a few times from alcohol; it then melted at 188–189° and gave no m. p. depression when mixed with crotonaldehyde 2,4-dinitrophenylhydrazone.

Found %: N 22.75, 22.78. Calc. for C₁₀H₁₀O₄N₄: Calculated %: N 22.38.

The diisoamylacetal of vinylacetaldehyde (V, R = iso-C₅H₁₁). A mixture of 10 ml of acetone, 0.5 g of mercuric acetate, and 0.2 g of boron trifluoride etherate was treated with 65 g of vinyl isoamyl ether, added at 0°, during 1.5 hr, with vigorous stirring. The reaction mixture was stirred for a further 1 hr at room temperature and then treated as in the previous experiment. The product was 52 g (80%) of the diisoamylacetal of vinylacetaldehyde.

B. p. 56–57° (0.5 mm); n_D^{20} 1.4273; d_4^{20} 0.8385; MR_D 69.98, calc. 69.87.

Found %: C 73.42, 73.98; H 12.43, 12.30. Calc. for C₁₄H₂₈O₂: Calculated %: C 73.63; H 12.36.

The dibutylacetal of vinylacetaldehyde (V, R = C₄H₉) was prepared in a similar way.

B. p. 102° (11 mm); n_D^{20} 1.4236; d_4^{20} 0.8477; MR_D 60.33, calc. 60.43.

Found %: C 72.07, 72.19; H 12.16, 12.17. Calc. for C₁₂H₂₄O₂: Calculated %: C 71.95; H 12.08.

The compounds V (R = C₄H₉ and iso-C₅H₁₁) gave the same crotonaldehyde 2,4-dinitrophenylhydrazone (mixed m. p.) on treatment with 2,4-dinitrophenylhydrazine sulfate.

Hydrogenation of the diethylacetal of vinylacetaldehyde. A 14.4 g sample of the diacetal was hydrogenated at 50° in the presence of Pd/CaCO₃ catalyst. The theoretical volume of hydrogen was absorbed in 30 hr. The product was filtered and redistilled, to give 13 g of the diethylacetal of butyraldehyde (b. p. 143–146°; n_D^{22} 1.3948). The 2,4-dinitrophenylhydrazone (m. p. 122–123° [10]) gave no m. p. depression when mixed with a known sample of butyraldehyde 2,4-dinitrophenylhydrazone.

Hydrolysis of the diethylacetal of vinylacetaldehyde. A mixture of 12.7 g of the diethylacetal of vinylacetaldehyde with 15 ml of 5% phosphoric acid was stirred vigorously for 5 hr at 60°. The reaction mixture was then diluted with ether, washed with water and with dilute sodium bicarbonate solution, and dried over sodium sulfate. The product was 4 g (64.7%) of crotonaldehyde (b. p. 102–104°; n_D^{18} 1.4324).

The 2,4-dinitrophenylhydrazone (m. p. 188–189°) gave no m. p. depression when mixed with crotonaldehyde 2,4-dinitrophenylhydrazone [11].

Condensation of the diethylacetal of vinylacetaldehyde with vinyl ethyl ether. A stirred mixture of 20 g of the diethylacetal of vinylacetaldehyde with 0.1 g of ferric chloride at 0° was treated with 4.9 g of vinyl ethyl ether, added over 45 min. The mixture was stirred for a further 2 hr at 20°, neutralized with sodium methoxide, and redistilled in vacuo. The product was 3.5 g (23.8%) of 1,1,3-triethoxyhexa-5-ene.

B. p. 50–52° (0.5 mm); n_D^{20} 1.4230; d_4^{20} 0.8852; MR_D 62.23, calc. 62.08.

Found %: C 66.60, 67.14; H 11.10, 11.17. Calc. for C₁₂H₂₄O₃: Calculated %: C 66.63; H 11.18.

1-Ethoxybuta-1,3-diene. A porcelain tube, 60 cm long and 20 mm in diameter, was packed with 100 ml of MgHPO₄·Na₂SiO₃ catalyst [12]; 34 g of the diethylacetal of vinylacetaldehyde was passed through this at 20 mm pressure, at 350°, during 80 min. The product was condensed out in a trap cooled by solid carbon dioxide and

acetone, washed with water, dried over anhydrous potash, and redistilled. The yield was 16.7 g (72.5%) of 1-ethoxybuta-1,3-diene (b. p. 65–67° at 150 mm; n_D^{20} 1.4610 [12]).

1-Butoxybuta-1,3-diene was obtained in a similar way from the dibutylacetal of vinylacetaldehyde (yield 70%).

B. p. 44–45° (8 mm); n_D^{20} 1.4619.

Found %: C 75.80, 76.09; H 11.42, 11.42. Calc. for $C_8H_{14}O$: Calculated %: C 76.14; H 11.18.

1-Isoamylxybuta-1,3-diene was obtained in 45% yield from the diisoamylacetal of vinylacetaldehyde.

B. p. 59–60° (10 mm); n_D^{20} 1.4610; d_4^{20} 0.8180; MR_D 47.02, calc. 44.47.

Found %: C 77.41, 77.33; H 11.62, 11.60. Calc. for $C_9H_{16}O$: Calculated %: C 77.09; H 11.50.

Dienic synthesis from 1-ethoxybuta-1,3-diene and maleic anhydride. A solution of 9.8 g of 1-ethoxybuta-1,3-diene in 30 ml of benzene was treated with 8.7 g of maleic anhydride. The reaction mixture was heated to boiling and allowed to stand for 5 hr. The product was redistilled in vacuo. The yield was 8 g of 2-ethoxy-1,2,5,6-tetrahydrophthalic anhydride (VIII, $R = C_2H_5$).

B. p. 141–142° (2 mm); n_D^{20} 1.4850; d_4^{20} 1.2081; MR_D 46.56, calc. 46.82.

Found %: C 61.54, 61.22; H 6.37, 6.39. Calc. for $C_{10}H_{12}O_4$: Calculated %: C 61.21; H 6.17.

2-Butoxy-1,2,5,6-tetrahydrophthalic anhydride (VIII, $R = C_4H_9$) was obtained in a similar way.

B. p. 129–130° (0.5 mm); n_D^{20} 1.4830; d_4^{20} 1.1385; MR_D 56.74, calc. 55.94.

Found %: C 64.53, 64.68; H 7.09, 7.10. Calc. for $C_{12}H_{16}O_4$: Calculated %: C 64.27; H 7.19.

2-Isoamylxy-1,2,5,6-tetrahydrophthalic anhydride (VIII, $R = \text{iso-C}_5H_{11}$) was obtained similarly.

B. p. 140–141° (0.5 mm); n_D^{20} 1.4808; d_4^{20} 1.1257; MR_D 60.20, calc. 60.55.

Found %: C 65.79, 65.70; H 7.78, 7.72. Calc. for $C_{13}H_{18}O_4$: Calculated %: C 65.53; H 7.61.

2-Ethoxy-1,2,5,6-tetrahydrophthalic acid (IX, $R = C_2H_5$) was obtained by boiling 4 g of the anhydride (VIII, $R = C_2H_5$) with 15 ml of water for 4 hr. The yield was 3.1 g (m. p. 138–138.5°, from water).

Found %: C 56.31, 56.22; H 6.74, 6.67. Calc. for $C_{10}H_{14}O_5$: Calculated %: C 56.07; H 6.59.

2-Butoxy-1,2,5,6-tetrahydrophthalic acid (IX, $R = C_4H_9$) was obtained similarly (m. p. 122–122.5°).

Found %: C 59.74, 59.91; H 7.64, 7.57. Calc. for $C_{12}H_{18}O_5$: Calculated %: C 59.45; H 7.49.

2-Isoamylxy-1,2,5,6-tetrahydrophthalic acid (IX, $R = \text{iso-C}_5H_{11}$) was obtained similarly (m. p. 125.5–126°).

Found %: C 60.98, 61.45; H 7.93, 8.06. Calc. for $C_{13}H_{20}O_5$: Calculated %: C 60.92; H 7.87.

SUMMARY

1. An investigation has been made of the autocondensation reactions of vinyl ethyl, vinyl butyl, and vinyl isoamyl ethers in the presence of the complex catalysts $BF_3 \cdot O(C_2H_5)_2 + HgO$, $BF_3 \cdot O(C_2H_5)_2 + Hg(OCOCH_3)_2$, etc. The acetals of vinylacetaldehyde are formed; the reaction mechanism is discussed.

2. These acetals of vinylacetaldehyde can easily be converted, in high yield, to 1-alkoxybuta-1,3-dienes.

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* Original Russian pagination. See C. B. translation.

REACTIONS OF HYDRAZINE DERIVATIVES

XXXI. SOME β -ARYLETHYLHYDRAZINES AND

THE CORRESPONDING HYDRAZONES

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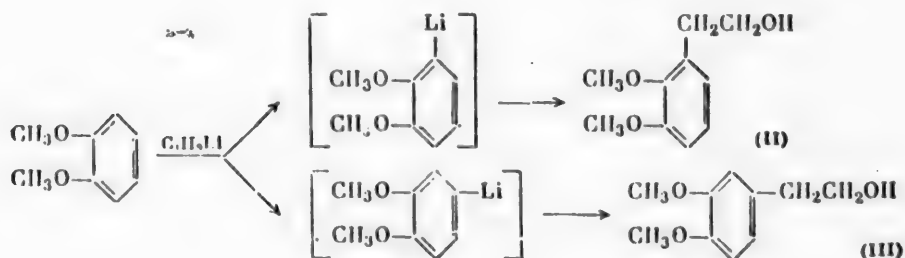
A number of investigators have recently devoted their attention to the synthesis of arylalkyl hydrazines in which the hydrazine group is in the β -position of the side chain, because β -phenylisopropylhydrazine has been found to be effective in reducing blood pressure [1].

β -Phenylethylhydrazine (I) itself has been synthesized in 41% yield by the direct alkylation of hydrazine [2]. N,N-di(β -phenylethyl)hydrazine is formed as a secondary product.



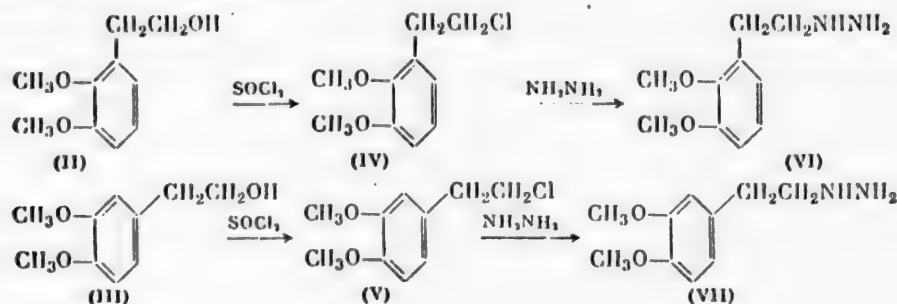
We repeated this synthesis, using the improved method developed for benzylhydrazine [3], and obtained β -phenylethylhydrazine (I) in 83% yield. The reaction was carried out with vigorous stirring without solvent. A difference from benzylhydrazine preparation was that it was necessary to heat the hydrazine hydrate to 90°.

It was of interest to synthesize some β -phenylethylhydrazines with methoxy groups in the benzene ring, in view of their structural relationships to alkaloids of the mescaline type. For this purpose it was necessary to obtain the corresponding dimethoxyphenylethyl chlorides, which could be conveniently synthesized from the corresponding alcohols. Such alcohols are usually obtained by diazotization of the corresponding amines or by reduction of esters [4-7]. By analogy with a method described [8] for the preparation of β -(2,5-dimethoxyphenyl) ethyl alcohol, we treated butyllithium with veratrole to obtain a mixture of the two isomers of veratryllithium, and this reacted with ethylene oxide to give a mixture of the corresponding alcohols.



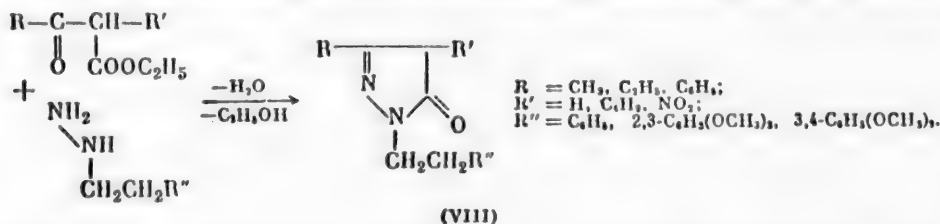
We were able to separate these alcohols by fractional distillation under reduced pressure, and thus to obtain β -(2,3-dimethoxyphenyl)ethyl alcohol (II) in 47% yield and β -(3,4-dimethoxyphenyl)ethyl alcohol (III) in 17% yield.

The corresponding chlorides (IV and V) were synthesized in 81–82% yield by reaction of the alcohols with thionyl chloride. Direct alkylation of hydrazine with these chlorides then gave two new monosubstituted dimethoxyphenylethylhydrazines (VI and VII).



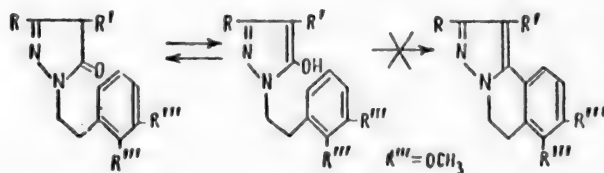
All the β -phenylethylhydrazines which we prepared were colorless oily liquids of high refractive index. They turned yellow and gave off nitrogen on standing exposed to air. Their hydrochlorides were readily obtained by passing hydrogen chloride through solutions of the hydrazines in anhydrous benzene or absolute ether.

These β -arylethylhydrazines were condensed with esters of β -keto acids to give 1-arylethylpyrazol-5-ones.

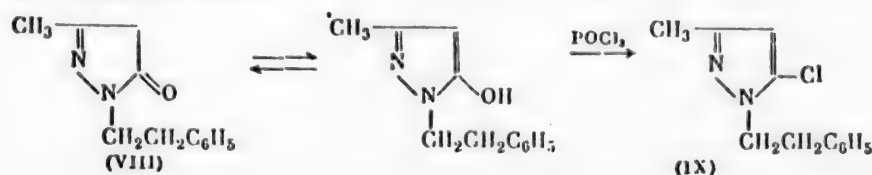


The condensation was carried out without solvent or with a small amount of alcohol, and, after a short heating period, the reaction mixture was diluted with a large quantity of ether; the crystalline pyrazolone then precipitated immediately in a reasonably pure state.

Considering that the pyrazolones should to some extent show the properties of cyclic amides, we carried out an experiment on cyclization, similar to the Bischler-Napieralskii reaction, by heating 1-arylethylpyrazolones with a dehydrating agent.



The dehydrating agents used were phosphorus pentoxide in various solvents or without solvent, polyphosphoric acid, and phosphorus oxychloride. In most cases there was no reaction. In the attempts to carry out cyclization with phosphorus oxychloride, the only reaction was substitution of the hydroxyl group of the enol form of the pyrazolone by halogen, e. g. the product from 1-(β -phenylethyl)-3-methylpyrazol-5-one was 1-(β -phenylethyl)-3-methyl-5-chloropyrazole (IX).



A similar reaction was observed with 1-[(2,3-dimethoxyphenyl)ethyl]-3-methylpyrazol-5-one.

Arguing that the introduction of a nitro group into the 4 position might activate the hydroxyl group and thus promote cyclization, we prepared the corresponding nitropyrazolone by a method similar to one described in the literature [9]. However, cyclization did not occur in this case either. The hydrogen in the benzene ring should be mobile under the influence of the methoxy groups, and the reason for the absence of cyclization is evidently the low mobility, or more precisely the acid character, of the hydroxyl group in the 5 position.

EXPERIMENTAL

β -Phenylethylhydrazine (I). A 520 g quantity of 96% hydrazine hydrate was heated on a water bath to 90°, and 140 g of β -phenylethylchloride was added, with vigorous stirring, over a period of 4 hr. Stirring was continued for another 2 hr at the same temperature. The mixture was then cooled to room temperature and extracted continuously with ether. The ether was distilled off from the extract, and the residue was redistilled in vacuo. The product was 103 g (83%) of β -phenylethylhydrazine (b. p. 132–136° at 10 mm). This had the following properties after two redistillations.

B. p. 134.5° (10 mm); n_D^{20} 1.5490; d_4^{20} 1.0161; MR_D 42.63, calc. for $C_8H_{12}N_2$ 42.68.

Literature data [2]: b. p. 137–139° (12–13 mm); yield 41%.

1-(β -Phenylethyl)-3-methylpyrazol-5-one (VIII, R = CH₃, R' = H, R'' = C₆H₅). A 27.3 g charge of β -phenylethylhydrazine was mixed, a little at a time, with 26.1 g of freshly distilled acetoacetic ester. The resulting warm mixture was heated for 30 min on a water bath, cooled to room temperature, and treated with 150 ml of ether. The yield was 32.1 g (80%), m. p. 139–140° (from alcohol) [10], λ_{max} 246 m μ , log ϵ 3.806 (in methanol).

1-(β -Phenylethyl)-3-methyl-4-nitropyrazol-5-one (VIII, R = CH₃, R' = NO₂, R'' = C₆H₅). A solution of 30.3 g of 1-(β -phenylethyl)-3-methylpyrazol-5-one in 50 ml of alcohol and 20 ml of concentrated hydrochloric acid was treated with 15.3 g of sodium nitrite in 200 ml of water. The solution turned yellow when the first part of the nitrite was added, and finally there was a precipitate of orange crystals of the nitroso derivative.

The resulting 1-(β -phenylethyl)-3-methyl-4-nitrosopyrazol-5-one [10] was suspended in a small amount of acetic acid and treated, drop by drop, with 30 ml of concentrated nitric acid. The reaction mixture was diluted with water when evolution of nitrogen oxide had ceased, and the crystalline precipitate was separated. Yield 33.7 g (91%), m. p. 140–141° (from alcohol).

Found %: N 16.41, 16.83. Calc. for $C_{12}H_{13}O_3N_3$: Calculated %: N 17.00.

1-(β -Phenylethyl)-3-ethylpyrazol-5-one (VIII, R = C₂H₅, R' = H, R'' = C₆H₅). A 2.7 g sample of β -phenylethylhydrazine was mixed slowly with 2.9 g of propionylacetic ester, using water cooling. The mixture was heated on a water bath for 40 min, and cooled to room temperature. The resulting oil was dissolved in 50 ml of ether, and allowed to stand overnight in the cold. The crystalline precipitate formed was separated and dried at 60°. Yield 2.8 g (65%), m. p. 98–99° (from alcohol).

Found %: N 12.92, 12.63. Calc. for $C_{13}H_{16}ON_2$: Calculated %: N 12.95.

1-(β -Phenylethyl)-3-methyl-4-butylpyrazol-5-one (VIII, R = CH₃, R' = C₄H₉, R'' = C₆H₅). A mixture of 27.2 g of β -phenylethylhydrazine and 37.4 g of α -butylacetoacetic ester was heated on a water bath for 40 min. The resulting oil was dissolved in 20 ml of ether and allowed to stand overnight in the cold. The crystals deposited were recrystallized from ether. Yield 23.5 g (46%), m. p. 82–83°.

Found %: N 10.82, 11.11. Calc. for $C_{16}H_{22}ON_2$: Calculated %: N 10.84.

1-(β -Phenylethyl)-3-phenylpyrazol-5-one (VIII, R = R'' = C₆H₅, R' = H). A 13.6 g sample of β -phenylethylhydrazine was mixed slowly with 19.2 g of benzoylacetic ester, using water cooling. The mixture was heated on a water bath for 1 hr, treated with the minimum quantity of alcohol required to dissolve the deposit, and cooled to give white crystals which were recrystallized from alcohol. Yield 21.9 g (83%), m. p. 144–145° [10].

Synthesis of β -(dimethoxyphenyl)ethyl alcohols (II and III). A liter flask was fitted with a stirrer, a dropping funnel, and a reflux condenser, and charged with 50 ml of anhydrous ether and 15 g of lithium. A solution of 90 g of freshly distilled butyl chloride in 150 ml of anhydrous ether was then added gradually, with continuous stirring, at such a rate that the reaction was not interrupted and the ether boiled gently. When most of the lithium

had dissolved and the reaction began to slow down appreciably, the flask was heated for 1-2 hr until no appreciable amount of unreacted lithium remained. The 110.5 g of freshly distilled veratrole in 400 ml of anhydrous ether was added, drop by drop, from the dropping funnel over a period of 1.5 hr. Stirring was continued for another hour, and the mixture was allowed to stand overnight. The flask was then cooled in ice and salt, 70 g of ethylene oxide was admitted over a 4 hr period with constant stirring, and the mixture was allowed to stand overnight. The product was then treated cautiously with 2 liters of iced water, and the upper organic layer was separated. The aqueous layer was extracted with ether, the extracts were combined with the organic layer, and this mixture was dried over sodium sulfate. The ether was distilled off on a water bath, and the residue was distilled in vacuo. The mixture of isomeric alcohols, which distilled between 150 and 170° (7 mm), was fractionated under reduced pressure to give two fractions.

First β -(2,3-dimethoxyphenyl)ethyl alcohol, yield 68.4 g (47%).

B. p. 151-152° (7 mm); n_D^{20} 1.5340; d_4^{20} 1.1284; MR_D 50.09, calc. for $C_{10}H_{14}O_3F_3$ 49.59.

p-Nitrobenzoate, m. p. 110-111° (from benzene).*

Second β -(2,3-dimethoxyphenyl)ethyl alcohol, yield 24.4 g (17%).

B. p. 166-168° (7 mm); n_D^{20} 1.5378; d_4^{20} 1.1403; MR_D 49.97, calc. for $C_{10}H_{14}O_3F_3$ 49.59.**

β -(2,3-Dimethoxyphenyl)ethyl chloride (IV). A 54.6 g quantity of β -(2,3-dimethoxyphenyl)ethyl alcohol was added, with stirring, to 60.7 g of thionyl chloride over a period of 1.5 hr, at room temperature. The excess of thionyl chloride was distilled off from a water bath, and the residue was distilled in vacuo. The distillate was washed with potash solution, dried over calcium chloride, and redistilled in vacuo. Yield 50.1 g (82%).

B. p. 128-130° (7 mm); n_D^{20} 1.5331; d_4^{20} 1.1501; MR_D 53.22, calc. for $C_{10}H_{13}O_2ClF_3$ 52.93.

β -(3,4-Dimethoxyphenyl)ethyl chloride (V). This was prepared in a similar way from 18.2 g of β -(3,4-dimethoxyphenyl)ethyl alcohol and 22 g of thionyl chloride. Yield 16.2 g (81%).

B. p. 141-143° (7 mm); n_D^{20} 1.5311; d_4^{20} 1.1627; MR_D 53.40, calc. for $C_{10}H_{13}O_2ClF_3$ 52.93.

β -(2,3-Dimethoxyphenyl)ethylhydrazine (VI). A 130 g quantity of 96% hydrazine hydrate was heated to 90° and stirred vigorously while 50.2 g of β -(2,3-dimethoxyphenyl)ethyl chloride was added over a period of 3 hr. Heating and stirring were continued for another 2 hr. The product was cooled to room temperature and extracted with ether in a liquid extractor. The ethereal extract was dried over caustic potash, the ether was distilled off, and the residue was distilled in vacuo. Yield 35.3 g (72%).

B. p. 168-170° (7 mm); n_D^{20} 1.5590; d_4^{20} 1.1300; MR_D 56.07, calc. 55.63.

Hydrochloride: m. p. 118-119° (from alcohol).

Found %: C 52.21, 52.26; H 7.57, 7.68. Calc. for $C_{10}H_{17}O_2N_2Cl$: Calculated %: C 51.61; H 7.36.

β -(3,4-Dimethoxyphenyl)ethylhydrazine (VII). This was prepared in a similar way from 10.1 g of β -(3,4-dimethoxyphenyl)ethyl chloride and 26 g of hydrazine hydrate. Yield 6.4 g (65%).

B. p. 177-179° (10 mm); n_D^{20} 1.5459; d_4^{20} 1.1258; MR_D 55.19, calc. 55.63.

Hydrochloride: m. p. 114-115° (from alcohol).

Found %: C 51.76, 51.61; H 7.16, 7.48. Calc. for $C_{10}H_{17}O_2N_2Cl$: Calculated %: C 51.61; H 7.36.

1-[β -(2,3-Dimethoxyphenyl)ethyl]-3-methylpyrazol-5-one (VIII, R = CH_3 , R' = H, R'' = 2,3- $C_6H_3(OCH_3)_2$). A 19.6 g quantity of β -(2,3-dimethoxyphenyl)ethylhydrazine was slowly mixed with 13.0 g of acetoacetic ester, using water cooling. The mixture was heated on a water bath for 40 min, treated with 50 ml of alcohol, and cooled. The crystals deposited were separated. Yield 22.8 g (87%); m. p. 154-155° (from alcohol); λ_{max} 247 m μ , log ϵ 3.620 (in methanol).

Found %: C 64.10, 64.13; H 7.03, 7.19. Calc. for $C_{14}H_{18}O_3N_2$: Calculated %: C 64.11; H 6.92.

* Literature data [7]: b. p. 125-128° (2 mm); p-nitrobenzoate m. p. 111-112°.

** Literature data [5]: b. p. 166-168° (7 mm); n_D^{20} 1.5409; d_4^{20} 1.1426.

1-[β -(3,4-Dimethoxyphenyl)ethyl]-3-methylpyrazol-5-one (VIII, R = CH₃, R' = H, R'' = 3,4-C₆H₃(OCH₃)₂). This was obtained in a similar way from 2.0 g of β -(3,4-dimethoxyphenyl)ethylhydrazine and 1.3 g of acetoacetic ester. Yield 2.1 g (81%); m. p. 95–96° (from alcohol).

Found %: C 64.14, 64.33; H 6.96, 7.02. Calc. for C₁₄H₁₀O₃N₂: Calculated %: C 64.11; H 6.92.

The reaction of 1-(β -phenylethyl)-3-methylpyrazol-5-one with phosphorus oxychloride. A spherical flask, fitted with a reflux condenser and a calcium chloride tube, was charged with 20.2 g of 1-(β -phenylethyl)-3-methylpyrazol-5-one and 60 g of phosphorus oxychloride. The mixture was heated to boiling, whereupon hydrogen chloride was evolved and the mixture gradually acquired a violet-red color. Heating was continued for 10 hr. The excess of phosphorus oxychloride was distilled off from a water bath under reduced pressure, and the residue was heated with 1 : 1 hydrochloric acid. The acid extract was filtered and treated with caustic potash solution till alkaline. The oil liberated was extracted with ether, the extract was dried over calcium chloride, the ether was distilled off from a water bath, and the residue was redistilled in vacuo. The yield was 12.2 g (55%) of 1-(β -phenylethyl)-3-methyl-5-chloropyrazole; this had the following constants after a second distillation.

B. p. 147.5–148° (7 mm); n_D^{20} 1.5462; d_4^{20} 1.1228; M_R 62.22, calc. 62.46; λ_{\max} 252 and 253 m μ , log ϵ 2.217 and 2.267 (in methanol).

Found %: C 65.71, 65.88; H 6.11, 6.04; N 12.85, 13.01; mol. wt. 202.0, 202.1. Calc. for C₁₂H₁₃N₂Cl: Calculated %: C 65.30; H 5.94; N 12.69; mol. wt. 220.7.

This substance was a colorless liquid, readily soluble in ether, alcohol, methanol, and other organic solvents, insoluble in water, but soluble in hydrochloric acid.

The reaction of 1-[β -(2,3-dimethoxyphenyl)ethyl]-3-methylpyrazol-5-one with phosphorus oxychloride. A mixture of 5.3 g of 1-[β -(2,3-dimethoxyphenyl)ethyl]-3-methylpyrazol-5-one and 30 g of phosphorus oxychloride was boiled for 40 hr under a reflux condenser fitted with a calcium chloride tube. The excess of phosphorus oxychloride was then distilled off from a water bath under reduced pressure, and the residue was heated with 1 : 1 hydrochloric acid. The acid extract was filtered and treated with dilute caustic soda solution till alkaline. The oil liberated was extracted with ether, the extract was dried over calcium chloride, the ether was distilled off, and the residue was distilled in vacuo. The product was 1.95 g (35%) of 1-[β -(2,3-dimethoxyphenyl)ethyl]-3-methyl-5-chloropyrazole.

B. p. 194–195° (11 mm); n_D^{20} 1.5450; d_4^{20} 1.1877; M_R 74.72, calc. 74.75; λ_{\max} 223 and 278 m μ , log ϵ 4.13 and 3.06.

Found %: C 59.59, 59.80; H 6.19, 6.03. Calc. for C₁₄H₁₇O₂N₂Cl: Calculated %: C 59.78; H 6.09.

The action of phosphorus pentoxide on 1-(β -phenylethyl)-3-methylpyrazol-5-one. A solution of 4 g of 1-(β -phenylethyl)-3-methylpyrazol-5-one in 40 ml of dry tetralin was boiled with 20 g of phosphorus pentoxide for 30 min. Another 20 g of phosphorus pentoxide was then added, and boiling was continued for a further hour. The tetralin was decanted off, the sticky residue was dissolved in water, and this aqueous solution was washed with ether. The aqueous layer was made alkaline to yield 3.2 g of a crystalline material of m. p. 136–137° (from benzene). This gave no m. p. depression with the original pyrazolone.

Found %: C 70.65, 70.93; H 6.98, 7.05; N 13.87, 13.89. Calc. for C₁₂H₁₄ON₂: Calculated %: C 71.24; H 6.99; N 13.86.

Similar results were obtained in experiments with 1-(β -phenylethyl)-3-phenylpyrazol-5-one, 1-(β -phenylethyl)-4-butylpyrazol-5-one, 1-(β -phenylethyl)-3-methyl-4-nitropyrazol-5-one, and 1-[β -(2,3-dimethoxyphenyl)ethyl]-3-methylpyrazol-5-one. In all cases the starting material was recovered unchanged, and there was no sign of any cyclization product.

The action of polyphosphoric acid on 1-(β -phenylethyl)-3-methylpyrazol-5-one. A mixture of 6.1 g of 1-(β -phenylethyl)-3-methylpyrazol-5-one and 32 g of polyphosphoric acid was heated in an oil bath at 180–200° for 6 hr. The mixture was then poured into hot water, and the resulting solution was made alkaline with caustic potash solution. The product (5.5 g) melted at 136–137° (from benzene), and gave no m. p. depression with the product from the previous experiment.

SUMMARY

1. Syntheses are described for β -phenylethylhydrazine, its methoxy substituted derivatives, and a number of 1-(β -arylethyl)pyrazol-5-ones.

2. It was found that these pyrazolones did not undergo a cyclization reaction of the Bischler-Napieralski type in the presence of phosphorus oxychloride, but that they were converted into chloropyrazoles.

No cyclization products were obtained using other condensing agents.

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POLYNUCLEAR HETEROCYCLIC COMPOUNDS

IV. THE INTERACTION BETWEEN BIS-DIMEDONYLMETHANES AND AMMONIUM ACETATE

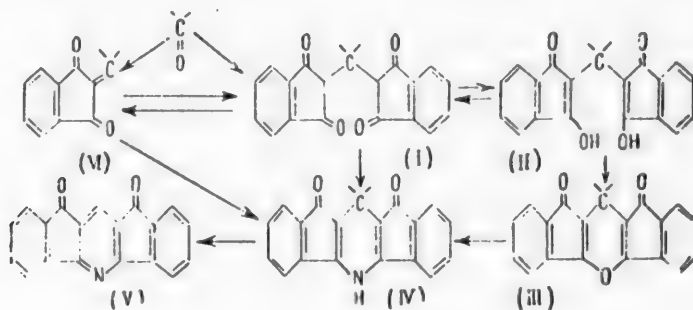
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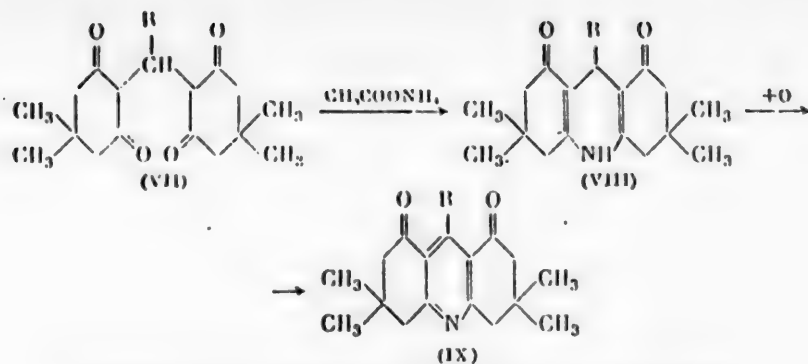
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It has been shown, in a number of papers [1-7] by one of the present authors and his collaborators that geminal bis-dioxoindanyl compounds (I) readily split off a water molecule from their enol forms (II) to give the corresponding pyrans (III), and these react with ammonia or primary amines to give the corresponding dihydropyridines (IV), which are often easily oxidized to pyridines (V). It has been shown that the pyran (III) stage can be bypassed and the dihydropyridine (IV) obtained directly by heating the geminal bis-dioxoindanyl compound (I) with ammonium acetate in glacial acetic acid [8], or more simply by heating the corresponding carbonyl compound with indan-1,3-dione and ammonium acetate [9]. When the carbonyl compound does not form a bis-dioxoindanyl derivative, it is possible to obtain the dihydropyridine (or pyridine) by heating the corresponding dioxoindanylidene methane derivative (IV) with ammonium acetate [10]. Thus, a general method has been developed for obtaining complex heterocyclic compounds - di(oxoindano)dihydropyridines - from indan-1,3-diones, carbonyl compounds and ammonium acetate.



It was of interest to apply this reaction to other cyclic β -diketones, firstly to cyclohexane-1,3-diones. It is known, for example, that dimedon (5,5-dimethylcyclohexane-1,3-dione) easily condenses with aldehydes; 1 molecule of aldehyde condenses with 2 molecules of cyclohexanedione, and the bis-dimedonylmethane formed is readily converted into the corresponding xanthene derivative. The latter reacts with ammonia or an amine to give a reduced acridine derivative. However, there is not much literature data [11-13] on similar reactions. An example is the preparation in poor yield of 3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,4-dione [12] by the action of alcoholic ammonia on tetramethyldecahydroxanthene, or of urotropine on dimedon.

We have investigated the reaction with ammonium acetate of some bis-dimedonylmethanes (VII), namely the condensation products of dimedon with formaldehyde (VIIa), benzaldehyde (VIIb), p-nitrobenzaldehyde (VIIc), and p-dimethylaminobenzaldehyde (VIId), and obtained good yields of the corresponding decahydroacridines (VIII).



The resulting tetramethyldecahydroacridinediones (VIIIa–VIIId) were yellow substances of high melting point (above 260°); they dissolved in alcoholic alkali with a deepening of color, and VIIIa and VIIIb then gave a strong green fluorescence.

A 1,4-dihydropyridine structure has been assumed in the literature on similar decahydroacridinediones without sufficient evidence. In most cases it has not even been proved that they are decahydroacridinediones, since the possibility of their oxidation to octahydroacridinediones (IXa–IXd) in the course of the reaction has not been excluded; there are examples of this in the literature [9, 10].

In order to establish the dihydropyridine structures of our products VIIIa to VIIId, the infrared spectra of their paraffin mulls were recorded between 3000 and 3500 cm⁻¹ (NaCl prism). All the spectra showed one or two absorption bands which were obviously attributable to valence vibrations of the N–H bond [14, 15].

Substance	λ_{\max} , cm ⁻¹
VIIIa	3181, 3274
VIIIb	3158, 3221
VIIIc	3330
VIIId	3137

Further precise identification of the 1,4-dihydropyridine structure and investigation of other regions in the spectra of these decahydroacridinediones will be pursued.

There is some information in the literature [16–17] on the oxidation of dihydropyridines to pyridines. Dihydropyridines obtained by Hantzsch's method are particularly easily oxidized. Vörländer [11] found that nitrous acid was

a convenient oxidizing agent for oxidizing decahydroacridinediones. We used his method for oxidizing our tetramethyldecahydroacridinediones (VIIIa–VIIId) to tetramethyloctahydroacridinediones (IXa–IXd). An oily substance was formed in the oxidation of VIIId to IXd, and this seriously interfered with the isolation of IXd in the pure state. The substance IXd was formed to some extent during the preparation of VIIId, showing that the latter was easily oxidized by atmospheric oxygen (or by disproportionation).

All the tetramethyloctahydroacridinediones IXa–IXd were white or pale yellow. Their melting points were considerably lower than those of the corresponding decahydroacridinediones (VIIIa–VIIId), and their solutions in alcoholic alkali showed no deepening of color. The infrared spectra of their paraffin mulls showed that the dihydropyridines had been oxidized to pyridines. Their infrared spectra in other regions will be investigated also.

The dioximes were prepared in order to characterize these tetramethyldecahydroacridinediones (VIII) and their oxidation products (IX). It was found that oxidation occurred during oxime formation, so that the oximes obtained from the decahydroacridinediones were those of the octahydroacridinediones. Thus identical oximes, giving no melting point depression on mixing, were obtained from VIIIa and IXa, and the same was true for the pairs of compounds VIIIb and IXb, and VIIId and IXd. However, IXa,b,d formed oximes more rapidly and easily than VIIIa,b,d.

EXPERIMENTAL

3,3,6,6,-Tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (VIIIa). a) A hot solution of 2 g of bis-dimedonylmethane (VIIa) [18] in 30 ml of glacial acetic acid was treated with 2.5 g of ammonium acetate (5-fold excess). The solution became orange-yellow. It was boiled for 30 min and water was added until a deposit appeared; the latter rapidly crystallized. The yield was 1.1 g (61%) of green-yellow shining crystals. Their m. p.

was 296–297° after recrystallization from dilute ethanol or methanol. A solution in ethanol showed a strong blue fluorescence, and solutions in concentrated sulfuric acid and in sodium methylate showed a strong green fluorescence. The product was insoluble in ether or benzene.

Found %: N 5.00. Calc. for $C_{17}H_{23}O_2N$: Calculated %: N 5.12.

b) A solution of 4.16 g of dimedon and 0.5 g of paraformaldehyde in 20 ml of glacial acetic acid was treated with 11 g of ammonium acetate, added a little at a time, boiled for 20 min, and subsequently treated as described under a). Yield 2 g (49%); m. p. 296–297°.

Found %: N 5.18. Calc. for $C_{17}H_{23}O_2N$: Calculated %: N 5.12.

3,3,6,6-Tetramethyl-1,2,3,4,5,6,7,8-octahydroacridine-1,8-dione (IXa). A solution of 1 g of VIIIa in 50 ml of 1 : 1 hydrochloric acid, cooled in ice water, was treated with sodium nitrite until the yellow color disappeared. The IXa formed precipitated in addition of alkali. M. p. 146° (from ethanol with addition of petroleum ether).

Found %: N 5.23. Calc. for $C_{17}H_{23}O_2N$: Calculated %: N 5.16.

Dioximes. A mixture of 1 g of VIIIa, 25 ml of pyridine, and 0.5 g of hydroxylamine hydrochloride was boiled for 1 hr and then poured into water acidified with hydrochloric acid. The yield was 0.9 g (80%) of the dioxime of IXa, in the form of white crystals; m. p. 280° (decomp.) (from ethanol). The same dioxime was obtained in similar way from IXa. A mixture of the two products showed no m. p. depression.

Found %: N 14.20. Calc. for $C_{17}H_{23}O_2N_3$: Calculated %: N 13.94.

3,3,6,6-Tetramethyl-9-phenyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (VIIIb). a) A solution of 5.8 g of bis-dimedonylphenylmethane (VIIb) in 80 ml of glacial acetic acid was treated with 6 g of ammonium acetate (5-fold excess), added a little at a time, boiled for 1 hr, and poured into water. There was a precipitate of 4 g (74%) of yellow crystals. The m. p. was 292° (decomp.) after recrystallization from ethanol. A solution in sodium ethylate showed a strong green fluorescence. A solution in concentrated sulfuric acid was yellow. The material was soluble in glacial acetic acid, but not in ether or benzene.

b) A solution of 12 g of dimedon and 6.6 ml of benzaldehyde in 30 ml of glacial acetic acid was treated with 8 g of ammonium acetate, added a little at a time, boiled for 1 hr, and subsequently treated as under a). Yield 11.2 g (75%); m. p. 292° (decomp.).

Found %: N 4.33. Calc. for $C_{23}H_{27}O_2N$: Calculated %: N 4.01.

Tetraacetate. A 1.5 g sample of VIIIb was dissolved, by heating gently, in 20 ml of acetic anhydride. The solution was cooled, treated with 10 drops of concentrated sulfuric acid, and allowed to stand for a few days during which a precipitate formed. The resulting tetraacetate was easily hydrolyzed back to VIIIb, even by boiling with alcohol. M. p. 220°.

Found %: N 2.56. Calc. for $C_{31}H_{39}O_8N$: Calculated %: N 2.53.

3,3,6,6-Tetramethyl-9-phenyl-1,2,3,4,5,6,7,8-octahydroacridine-1,8-dione (IXb). A solution of VIIIb in a mixture of acetic acid and hydrochloric acid was cooled in ice water and treated with sodium nitrite until the color disappeared. The resulting IXb was precipitated by addition of alkali. White crystals of m. p. 218° (from ethanol). No coloration was obtained with sodium ethylate.

Found %: N 4.30. Calc. for $C_{23}H_{25}O_2N$: Calculated %: N 4.03.

Dioximes. A mixture of 3 g of VIIIb, 30 ml of pyridine, and 1 g of hydroxylamine hydrochloride was boiled for 4 hr and poured into water. The dioxime of IXb was precipitated as white crystals; m. p. 250° (decomp.) (from water + dioxane). The same dioxime was obtained in a similar way from IXb. A mixture of the two products showed no m. p. depression.

Found %: N 11.46. Calc. for $C_{23}H_{27}O_2N_3$: Calculated %: N 11.13.

3,3,6,6-Tetramethyl-9-p-nitrophenyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (VIIIc). a) A solution of 6.6 g of p-nitrophenyl-bis-dimedonyl methane (VIIc) in 10 ml of glacial acetic acid was treated with 8 g of ammonium acetate, added a little at a time, and the resulting brown-red solution was boiled for 30 min.

Yellow crystals were deposited; yield 4.1g (66%); m. p. 279–280° (decomp.) (from ethanol). A solution in sodium ethylate was orange colored.

Found %: N 7.30. Calc. for $C_{23}H_{26}O_4N_2$: Calculated %: N 7.10.

b) A solution of 12 g of dimedon and 6 g of p-nitrobenzaldehyde in 36 ml of glacial acetic acid was treated with 8 g of ammonium acetate, added a little at a time, and boiled for 30 min. The yield was 11.7 g (69%); m. p. 279–280° (decomp.).

Found %: N 7.35. Calc. for $C_{23}H_{26}O_4N_2$: Calculated %: N 7.10.

3,3,6,6-Tetramethyl-9-p-nitrophenyl-1,2,3,4,5,6,7,8-octahydroacridine-1,8-dione (IXc). This was obtained in a similar way to IXb. White crystals; m. p. 250–252°.

Found %: N 6.95. Calc. for $C_{23}H_{24}O_4N_2$: Calculated %: N 7.14.

3,3,6,6-Tetramethyl-9-p-dimethylaminophenyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (VIIIId).

a) The method of preparation was similar to a) for VIIIc. The yield from 2 g of p-dimethylaminophenyl-bis-dimedonylmethane, 5 ml of glacial acetic acid, and 1.6 g of ammonium acetate was 0.8 g (42%) of yellow crystals (from dilute acetic acid), of m. p. 293–294° (decomp.). A solution in concentrated sulfuric acid showed a strong green fluorescence, a solution in sodium ethylate was yellow colored.

Found %: N 7.26. Calc. for $C_{25}H_{32}O_2N_2$: Calculated %: N 7.14.

b) The method of preparation was similar to b) for VIIIc. The yield from 6 g of dimedon, 3 g of p-dimethylaminobenzaldehyde, 18 ml of glacial acetic acid, and 6 g of ammonium acetate was 4.7 g (56%) of yellow crystals. The melting point was 293–294° (decomp.) after crystallization from acetic acid or ethanol.

Found %: N 7.43. Calc. for $C_{25}H_{32}O_2N_2$: Calculated %: N 7.14.

Hydrochloride. Some VIIIId was dissolved in concentrated hydrochloric acid and the solution evaporated. The resulting yellow crystals were readily soluble in water; concentrated solutions were yellow, dilute solutions showed a strong blue fluorescence. The salt was soluble in alcohol.

Found %: N 5.59; HCl 14.75. Calc. for $C_{25}H_{32}O_2N_2 \cdot 2HCl$: Calculated %: N 6.01; HCl 15.67.

3,3,6,6-Tetramethyl-9-p-dimethylaminophenyl-1,2,3,4,5,6,7,8-octahydroacridine-1,8-dione (IXd). a) In some cases, during the production of VIIIId, a white crystalline material was obtained on dilution of the reaction mixture with water. M. p. 147–148° (from ethanol). This dissolved in concentrated sulfuric acid without any coloration.

Found %: N 7.48. Calc. for $C_{25}H_{30}O_2N_2$: Calculated %: N 7.17.

b) A sample of VIIIId was dissolved in a mixture of glacial acetic and hydrochloric acid and oxidized with sodium nitrite as described above. The resulting light brown precipitate was recrystallized from ethanol or dilute aqueous acetone to give yellow crystals of m. p. 145–146°. A similar product was obtained by oxidation with chromic anhydride, sodium persulfate, or hydrogen peroxide in glacial acetic acid. These products showed the same infrared spectrum as that obtained under a).

Found %: N 6.86. Calc. for $C_{25}H_{30}O_2N_2$: Calculated %: N 7.17.

Dioximes. The same dioxime was obtained, by the procedure described above, from both VIIIId and IXd; this was in fact the dioxime of IXd. Recrystallization from ethanol or dilute acetic acid gave white crystals of m. p. 297°.

Found %: N 13.78. Calc. for $C_{25}H_{32}O_2N_4$: Calculated %: N 13.32.

SUMMARY

The 3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-diones, obtained by reaction of ammonium acetate with bis-dimedonylmethane, phenyl-bis-dimedonylmethane, p-nitrophenyl-bis-dimedonylmethane, and p-dimethylaminophenyl-bis-dimedonylmethane in glacial acetic acid, are easily oxidized to the corresponding 1,2,3,4,5,6,7,8-octahydroacridine-1,8-diones. Only the dioximes of the octahydroacridinediones are obtained by reaction with hydroxylamine of the decahydro- and octahydro-acridinediones.

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SYNTHESIS OF 2- AND 3-ALKYL-1-THIAINDANES

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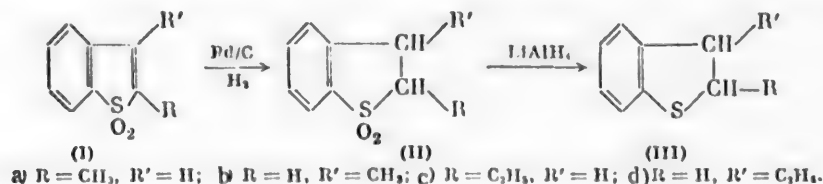
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In searching for methods for the preparative synthesis of alkyl-1-thiaindanes, we succeeded in obtaining a good yield of 3-methyl-1-thiaindane (IIIb) [1]. A special feature of the method was the two-stage selective hydrogenation of thiaindenesulfones (I). There was, therefore, a need for studying the possible wider use of selective hydrogenation for the synthesis of various alkyl-1-thiaindanes.

In this paper we describe preparative syntheses of 1-methyl-1-thiaindane (IIIa), 2-ethyl-1-thiaindane (IIIc), and 3-ethyl-1-thiaindane (IIId) by selective hydrogenation of 2- and 3-alkylthiaindenesulfones.

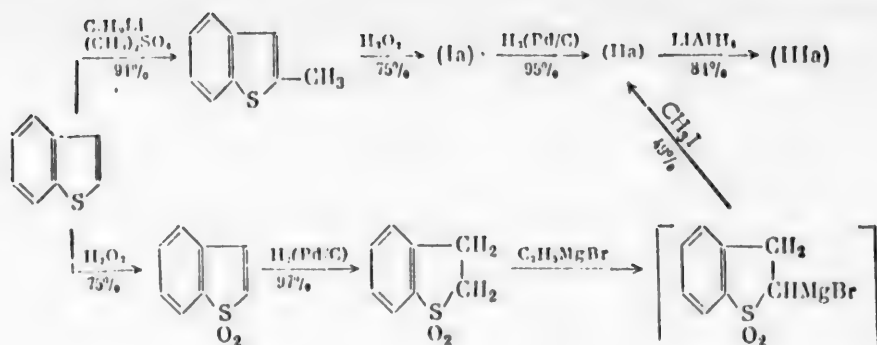


It is obvious that this method of selective hydrogenation of thiaindenesulfones could also be used for preparing alkyl-1-thiaindanes with alkyl substituents in the benzene ring.

2-Methyl-1-thiaindane (2-methyl-2,3-dihydrothianaphthene) (IIIa) had not been prepared before. There is a literature statement [2] that a fraction of b. p. 103–108° (8 mm) and n_D 1.5811 was isolated from the pyrolysis products of allyl phenyl sulfide, and, with very little justification, this was assigned the structure 2-methyl-1-thiaindane. However, we have shown [3] that only propenyl phenyl sulfide and its condensation products are obtained by pyrolysis of allyl phenyl sulfide, and it is probable that the fraction believed to be IIIa was really unpurified propenyl phenyl sulfide.

We obtained 2-methyl-1-thiaindane in two ways. In the first method, thiaindene was converted via its lithium derivative to 2-methylthiaindene and then to the sulfone (Ia). This was then selectively reduced in two stages, over palladium on charcoal to IIa and with lithium aluminum hydride to IIIa. In the second method, thiaindene was first oxidized to thiaindenesulfone, and this was selectively reduced to 1-thiaindanesulfone, which was converted to IIa by transmetallization [4] with ethylmagnesium bromide and subsequent treatment with methyl iodide. The two samples of IIa were identical. Conversion of IIa to IIIa was achieved, as before, with lithium aluminum hydride.

Both syntheses and the yields of different stages are shown on the following page.



It was found that the yields of 2-alkylthiaindenes obtained by the alkylation of 2-lithiumthiaindenes with dialkyl sulfates were considerably higher than those obtained by alkylation with alkyl halides or with *p*-toluenesulfonates.

2-Ethyl-1-thiaindane (IIIc) was prepared in the same way as IIIa. This substance has been obtained previously [5] in 16% yield by pyrolysis of *S*-crotylthiosalicylic acid, and by a different synthesis. However, neither of the products described were pure: the pyrolysis product had n_D^{20} 1.5714 and the product from reduction of 2-ethyl-3-hydroxythiaindene had n_D^{20} 1.5840 (in the latter case 2-ethylthiaindene was a probable impurity).

We synthesized the previously undescribed 2-ethylthiaindene by metallization of thiaindene with *n*-butyllithium and subsequent alkylation with diethyl sulfate. The product was oxidized to 2-ethylthiaindenesulfone (Ic), which was then selectively reduced in stages to 2-ethyl-1-thiaindane (IIIc).

3-Ethyl-1-thiaindane (IIId) has not been described before, and a previous attempt to synthesize it was unsuccessful [5]. 3-Ethylthiaindenesulfone (Id) was obtained by the method previously described [1] for 3-methylthiaindenesulfone (Ib). Propionyl bromide was converted via diazomethyl ethyl ketone [6] to bromomethyl ethyl ketone; this was condensed with sodium thiophenolate to give the previously unknown 1-phenylthiobutane-2-one, and this was cyclized by phosphorus pentoxide to give 3-ethylthiaindene. The latter was oxidized to Id, and reduced in stages to IIId and IIIId.

This method of synthesis excluded the possibility of obtaining an isomer of IIId with the substituent in the 2 position. The structure of IIId was further confirmed by hydrodesulfurization over Raney nickel to *sec*-butylbenzene, in almost quantitative yield.

3-Ethyl-1-thiaindanesulfone (IIId) has been described before [5]. However, on the basis of [7], it must have contained as impurity a significant amount of isomer with the substituent in the 2 position. Actually, the samples of 3-ethylthiaindenesulfone and 3-ethyl-1-thiaindanesulfone described in [5] melted at 130–131° and 37.5–38° respectively, whereas our products melted at considerably higher temperatures, namely 150° and 75–76° respectively. A mixture of equal quantities of 2-ethyl- and 3-ethyl-1-thiaindanesulfones melted at 33–42°, and a 70:30 mixture of 3-ethyl- and 2-ethyl-isomers melted at 40–46°. Hence the 3-ethyl-1-thiaindanesulfone described in [5] must have contained not less than 25% of the 2-ethyl-isomer.

EXPERIMENTAL

Synthesis of 2-methyl-1-thiaindane (IIIa). Thiaindene (0.18 mole) was metallized with butyllithium [8]. An ethereal solution of the 2-lithiumthiaindene was treated with a solution of 0.18 mole of dimethyl sulfate in 100 ml of ether, stirred for 1 hr, and boiled for 0.5 hr. The ether was distilled off, and the residue was treated with sodium ethylate in alcohol (from 0.1 g-at of sodium and 120 ml of alcohol) and boiled for 0.5 hr. The mixture was treated with water and the ether layer separated. The ether extract was dried, the ether was distilled off, and the residue was distilled in vacuo to give 2-methylthiaindene. The yield was 91%; b. p. 92–93° (5 mm); m. p. 51–52° (lit. 51.5–52° [8]). The 2-methylthiaindene (0.14 mole) in glacial acetic acid was oxidized with 200% excess of 27% H_2O_2 for 1 hr at 100°. The product was a 75% yield of 2-methylthiaindenesulfone (Ia), of m. p. 109–110°.

* Melting points and boiling points were uncorrected for emergent stem.

Found %: C 59.69; H 4.44; S 17.47. Calc. for $C_9H_8O_2S$: Calculated %: C 60.00; H 4.44; S 17.77.

Ia (0.055 mole) was dissolved in 700 ml of alcohol and hydrogenated in the presence of 3 g of 5% palladium on carbon, with an initial hydrogen pressure of 50 atm, for 10 hr. Most of the alcohol was then distilled off, the residue was diluted with water, whereupon 2-methyl-1-thiaindanesulfone (IIa) precipitated. The yield was 95%; m. p. 115–115.5° (from alcohol).

Found %: C 59.38; H 5.53; S 17.67; mol. wt. 182. Calc. for $C_9H_{10}O_2S$: Calculated %: C 59.34; H 5.49; S 17.58; mol. wt. 182.

IIa (0.15 mole) was dissolved in benzene and treated with an ethereal solution of 0.23 mole of lithium aluminum hydride, so that the mixture boiled gently. The mixture was then stirred for 2 hr, diluted with water, and distilled in steam, and the distillate was extracted with ether. The ether extract was dried over magnesium sulfate, the ether was distilled off, and 2-methyl-1-thiaindane (IIIa) was obtained by distillation in vacuo. The yield was 81%; b. p. 118–120° (21 mm); $n_D^{20.5}$ 1.5905.

The IIIa was purified by heating it with alcoholic mercuric chloride to form a complex; yield 80%; m. p. 115–116°. The complex was decomposed with 15% hydrochloric acid, and the resulting mixture was steam distilled to give a 45% yield of purified IIIa.

B. p. 123° (24.5 mm); n_D^{20} 1.5922; d_4^{20} 1.0859; MR_D 46.76, calc. 45.94.

Found %: C 72.04; H 6.70; S 21.08; mol. wt. 149.8. Calc. for $C_9H_{10}S$: Calculated %: C 72.00; H 6.66; S 21.33; mol. wt. 150.

A second purification of IIIa via the complex produced no further change in physical properties.

Oxidation of IIIa with hydrogen peroxide (1 hr at 100°) gave the sulfone IIa; yield 70%; m. p. 115–116° (from alcohol). This product gave no melting point depression when mixed with a sample of IIa made from Ia.

Second synthesis of 2-methyl-1-thiaindanesulfone (IIa). Thiaindene was oxidized with H_2O_2 to give a 75% yield of thiaindenesulfone; m. p. 141–142.5° (from alcohol) (lit. m. p. 142–143° [9]).

Thiaindenesulfone (0.42 mole) in alcohol was hydrogenated for 4.5 hr in the presence of 3.5 g of 5% palladium on carbon, at an initial hydrogen pressure of 20 atm. The yield was 97% of 1-thiaindanesulfone; m. p. 90–91° (from alcohol) (lit. m. p. 91–92° [4]).

An ethereal solution of ethylmagnesium bromide (from 0.037 g-at of magnesium and 0.037 mole of ethyl bromide in 50 ml of ether) was treated with 0.03 mole of 1-thiaindanesulfone in 100 ml of benzene, boiled for 5 min, and treated with 0.045 mole of methyl iodide. The mixture was boiled for 4 hr and then treated with water and extracted with benzene. The benzene-ether extract was dried over ignited magnesium sulfate, the solvent was distilled off, and the residue was twice recrystallized from alcohol. The yield of IIa was 49%; m. p. 114–115°. This product gave no melting point depression when mixed with a sample of IIa obtained by hydrogenating Ia.

Synthesis of 2-ethyl-1-thiaindane (IIIc). An ethereal solution of 2-lithiumthiaindene, obtained from 0.05 mole of thiaindene as described above, was treated with 0.075 mole of diethyl sulfate in 50 ml of ether. The mixture was boiled for 10 hr, and then treated as in the synthesis of 2-methylthiaindene. The yield of 2-ethylthiaindene was 81%.

B. p. 95–96° (1.5 mm); n_D^{20} 1.6063; d_4^{20} 1.0870; MR_D 51.41, calc. 50.18.

Found %: C 73.93; H 6.31; S 19.72. Calc. for $C_{10}H_{10}S$: Calculated %: C 74.07; H 6.17; S 19.75.

The 2-ethylthiaindene was oxidized in the same way as 2-methylthiaindene to give a 77% yield of 2-ethylthiaindenesulfone (Ic); m. p. 86.5–87.5° (from alcohol).

Found %: C 61.86; H 5.14; S 16.31. Calc. for $C_{10}H_{10}O_2S$: Calculated %: C 61.86; H 5.16; S 16.49.

Ic (0.02 mole) was dissolved in 300 ml of alcohol and hydrogenated for 10 hr, in the presence of 2 g of 5% palladium on carbon, at 20°, at an initial hydrogen pressure of 50 atm. The catalyst was removed, the bulk of the alcohol was distilled off, and the residue was diluted with water, whereupon 2-ethylthiaindanesulfone (IIc) precipitated. The yield was 97%; m. p. 76–77° (from alcohol) (lit. m. p. 71–73° [5]).

Found %: C 61.30; H 6.11; S 16.03. Calc. for $C_{10}H_{12}O_2S$: Calculated %: C 61.22; H 6.12; S 16.32.

Unpurified IIc (0.07 mole) was dissolved in 200 ml of a mixture of ether and benzene (1 : 1) and treated with a solution of 0.11 mole of lithium aluminum hydride in 160 ml of ether, added at such a rate that the mixture boiled gently. Stirring was then continued for 2 hr, and the further treatment was as in the reduction of IIa. The yield of 2-ethyl-1-thiaindane (IIc) was 80.1%; b. p. 138–141° (26 mm); n_D^{20} 1.5790.

A mixture of 0.061 mole of IIc and 0.305 mole of mercuric chloride in 245 ml of alcohol was boiled for half an hour and then cooled in a mixture of ice and salt; the complex was precipitated in 78% yield; m. p. 79–80°. The complex was shaken up with 75 ml of isooctane at 20°, and filtered off under suction. It was then decomposed with an excess of 15% hydrochloric acid, and the mixture was steam distilled. The distillate was extracted with ether, the ether extract was washed with bicarbonate solution and with water, and dried over ignited magnesium sulfate, and the ether was distilled off. Distillation of the residue in vacuo gave purified IIc in 50% yield.

B. p. 136–137.2° (25 mm), 100.5° (4 mm); n_D^{20} 1.5790; d_4^{20} 1.0628; MR_D 51.28, calc. 50.65.

Lit. [5]: b. p. 69–72° (0.7–0.8 mm); n_D^{20} 1.5714; b. p. 130–133° (14 mm); n_D^{20} 1.5840.

Found %: C 73.31; H 7.39; S 19.40. Calc. for $C_{10}H_{12}S$: Calculated %: C 73.17; H 7.32; S 19.51.

IIc, of m. p. 74–76°, was reformed by oxidation of IIc with excess of H_2O_2 in glacial acetic acid, for 1 hr, at 100°. The product gave no melting point depression when mixed with a sample of IIc, prepared from Ic.

Synthesis of 3-ethyl-1-thiaindane (IIId). A cold (0°) solution of diazomethane in 700 ml of ether, obtained from 0.6 mole of nitrosomethylurea, was treated with 0.17 mole of propionyl bromide and stirred for 0.5 hr at 0°. Dry hydrogen bromide was then passed through for 6 hr at 0°, and the solution was stirred for 0.5 hr at the same temperature, washed with water and with bicarbonate solution, treated with magnesium oxide, and dried over ignited magnesium sulfate. The solvent was distilled off, and the residue was distilled from magnesium oxide to give a 34% yield of bromomethyl ethyl ketone; b. p. 152–155°; n_D^{20} 1.4656. Lit. [6]; yield 55%; b. p. 154–155°; n_D^{20} 1.4670.

A solution of 0.26 mole of thiophenol in 45 g of 30% caustic soda solution was treated with 0.24 mole of bromomethyl ethyl ketone at 20–25°, stirred for 1 hr, diluted with water, and extracted with ether. Distillation of the extract gave a 73.7% yield of 1-phenylthiobutan-2-one.

B. p. 156–157.5° (21 mm); m. p. 32–33.5° (from alcohol).

Found %: C 66.63; H 6.56; S 17.60. Calc. for $C_{10}H_{12}OS$: Calculated %: C 66.6; H 6.66; S 17.77.

1-Phenylthiobutan-2-one (0.03 mole) was heated with 0.014 mole of P_2O_5 for 45 min at 180–190° (unlike phenyl acetonyl sulfide [10], there was only partial cyclization at lower temperature). The cooled mixture was treated with water and extracted with ether, and the ether extract was washed with 20% caustic soda solution and with water, and dried over ignited magnesium sulfate. Distillation gave an 82% yield of 3-ethylthiaindene.

B. p. 110–111° (6 mm), 143° (24 mm); n_D^{20} 1.6068; d_4^{20} 1.1003; MR_D 50.83, calc. 50.18.

Lit. [5]: b. p. 130–131° (10 mm); n_D^{20} 1.6028.

Found %: C 74.27; H 6.33; S 19.44. Calc. for $C_{10}H_{10}S$: Calculated %: C 74.07; H 6.17; S 19.75.

3-Ethylthiaindene (0.043 mole) was oxidized by heating with 100% excess of 30% H_2O_2 in acetic acid, for 1 hr, at 70°. Dilution with water then precipitated a 78% yield of 3-ethylthiaindenesulfone (Id); m. p. 150° (from alcohol) (lit. [5] m. p. 130–131°).

Found %: C 61.86; H 5.08; S 16.33. Calc. for $C_{10}H_{10}O_2S$: Calculated %: C 61.85; H 5.16; S 16.49.

Id (0.044 mole) was dissolved in 600 ml of alcohol and hydrogenated over 4.5 g of 5% palladium on carbon, for 10 hr, at 20, with an initial hydrogen pressure of 50 atm. The product was filtered, the solvent was distilled off, and the oily residue of 3-ethylthiaindenesulfone (IIc) crystallized after prolonged cooling. The yield was 91%; m. p. 75–76° (from 1 : 1 aqueous alcohol) (lit. [5] m. p. 37.5–38°).

Found %: C 61.19; H 6.21; S 16.27. Calc. for $C_{10}H_{12}O_2S$: Calculated %: C 61.22; H 6.12; S 16.32.

A solution of 0.04 mole of IIId in 100 ml of 1 : 1 ether-benzene mixture was treated with 0.07 mole of lithium aluminum hydride dissolved in 100 ml of ether, at such a rate that the ether boiled gently. The mixture

was stirred for 2 hr at 20° and then treated as in the synthesis of IIIc. The yield was 90% of 3-ethyl-1-thiaindane (IIId); b. p. 144–145° (25 mm); n_D^{20} 1.5819.

The IIId was purified by mixing 0.036 mole with a solution of 0.19 mole of mercuric chloride in 152 ml of alcohol and boiling for 0.5 hr. An 87% yield of complex precipitated on cooling; m. p. 134–135° (from alcohol). This was extracted with 50 ml of isooctane at room temperature, filtered off, and decomposed with 1 : 1 hydrochloric acid. The mixture was steam distilled, and IIId was extracted from the distillate with ether. The yield was 49%.

B. p. 138–138.5° (25 mm); n_D^{20} 1.5833; d_4^{20} 1.0736; MR_D 51.07, calc. 50.65.

Found %: C 73.18; H 7.41; S 19.38. Calc. for $C_{10}H_{12}S$: Calculated %: C 73.17; H 7.32; S 19.51.

IIId (0.001 mole) was oxidized with 100% excess of 30% H_2O_2 in acetic acid by heating to 100° for 45 min. The product was diluted with water, and a 60% yield of IIb precipitated on cooling; m. p. 75–76°. This gave no melting point depression when mixed with a sample of IIb produced by hydrogenating Id.

IIId (0.01 mole) in 50 ml of alcohol was boiled for 10 hr with Raney nickel from 50 g of alloy. The mixture was then diluted with 50 ml of water and 40 ml of alcohol and distilled to dryness, and the residue was treated with 20 ml of water and 30 ml of alcohol and again distilled to dryness. A 97% yield of sec-butylbenzene was determined spectrophotometrically* in the distillate.

SUMMARY

Preparative methods have been developed for the synthesis of methyl- and ethyl-thiaindanes, using selective two-stage hydrogenation of the sulfones of the corresponding thiaindenes.

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* This determination was carried out by T. S. Novozhilova, using a "Uvispek" ultraviolet spectrophotometer.

** Original Russian pagination. See C. B. translation.

INVESTIGATIONS INTO THE CHEMISTRY OF 5-HALOGENOFURANS

XIV. THE INTERACTION OF 5-HALOGENOFURYLNITROETHYLENES

WITH METALLIC THIOCYANATES

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pp. 3297-3299, October, 1960

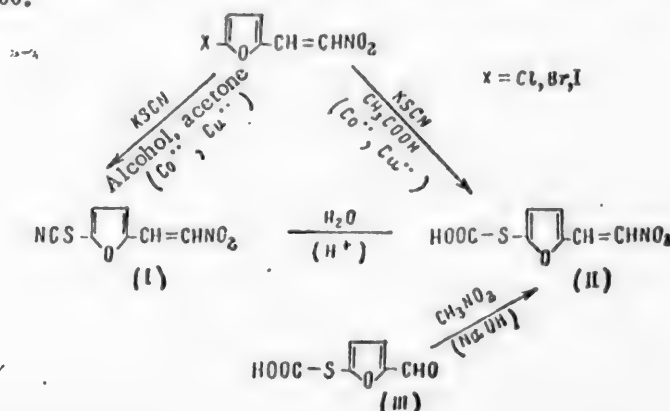
Original article submitted December 11, 1959

We previously [1] investigated the interaction of 5-halogenofurfurols with metallic thiocyanates. However, we did not succeed in obtaining 5-thiocyanatofurfurol in the pure state, because furfurol with a thiocyanato group in the 5 position was found to be of poor stability.

Assuming that 5-thiocyanatofurylnitroethylene (I) would be more stable, we investigated the possibility of an exchange reaction between halogen and thiocyanate by the interaction of 5-halogenofurylnitroethylenes with metallic thiocyanates in various solvents. The successful achievement of this reaction has led to the development of a new group of physiologically active substances, namely sulfur derivatives of ω -nitrovinylfuran.

We investigated the interaction of 5-halogenofurylnitroethylenes with the thiocyanates of potassium, sodium, silver, mercury, and lead in various solvents. It was found that, as in the case of 5-halogenofurfurols, replacement of bromine by thiocyanate only took place in the presence of catalysts, namely salts of copper or cobalt. When the reaction was carried out in anhydrous neutral solvents (acetone, methanol, ethanol), a crystalline product (I) was formed, which, as was expected, was considerably more stable than 5-thiocyanatofurfurol. It could be recrystallized easily from petroleum ether, methanol, ethanol, and other neutral solvents. When the exchange reaction was carried out in acetic acid, the result was a hydrolysis product of I, namely 2-(β -nitrovinyl)furan-5-ylthiocarboxylic acid (II). II was also readily obtained by hydrolyzing I by heating in an acid medium. Not only 5-bromo- and 5-iodo- but also 5-chlorofurylnitroethylene reacted with KSCN or NaSCN in acetic acid, in the presence of a trace of $\text{Co}(\text{SCN})_2$, to give II. It is noteworthy that we had previously been unable to replace the chlorine in 5-chloro derivatives of furan [2]. II was also obtained by condensing 2-formylfuran-5-ylthiocarboxylic acid (III) with nitromethane in the presence of NaOH and methanol.

The new compounds were investigated as bacteriocides. Tests showed that 5-thiocyanatofurylnitroethylene (I) had considerable bacteriocidal activity; it suppressed microbial growth (anthrax bacillus and staphylococcus) at a dilution of 1 : 10 000.



EXPERIMENTAL

5-Thiocyanatofurylnitroethylene (I). a) A mixture of 4 g of 5-bromofurylnitroethane, 4 g of anhydrous KSCN, and a few crystals of cupric thiocyanate in 50 ml of anhydrous acetone was heated for 22 hr on a water bath. The precipitated KBr was removed at intervals. The total weight of this precipitate was 1.7 g (77.9%). The filtrate was diluted with water and allowed to stand for 24 hr. The brown precipitate which formed on standing was recrystallized from a 20 : 1 mixture of ether and benzene, in the presence of charcoal. The yield was 2.7 g of yellow light crystals; m. p. 74.5°.

Found %: S 16.25, 16.07; N 13.89, 13.71. Calc. for $C_7H_4O_3N_2S$: Calculated %: S 16.34; N 14.27.

The use of $Co(SCN)_2$ as catalyst increased the yield to 85%.

b) A mixture of 1 g of 5-bromofurylnitroethylene, 1 g of NaSCN, and a few crystals of $Co(SCN)_2$ in 20 ml of anhydrous methanol was heated on a water bath, under a reflux condenser, for 10 hr. The precipitated NaBr was removed, and the filtrate was diluted with water. The yellow precipitate of unchanged 5-bromofurylnitroethylene was removed, and the filtrate was allowed to stand for 36 hr, when yellow crystals of I deposited. The yield was 0.8 g (83%); m. p. 74° (from mixture of petroleum ether and benzene). The yield of I was 74% when $Cu(SCN)_2$ or anhydrous $CuSO_4$ was used as catalyst.

2-(β -Nitrovinyl)furan-5-ylthiocarboxylic acid (II). a) A mixture of 4 g of 5-bromofurylnitroethylene, 5 g of NaSCN, and 50 ml of glacial acetic acid was heated on an oil bath until a yellow precipitate (polythiocyanogen) appeared; a few crystals of $Cu(SCN)_2$ or $Co(SCN)_2$ were then added, and the mixture was boiled on the oil bath for a further 40 min. The hot solution was filtered, the residue was washed with hot acetic acid, and the filtrate was poured into warm water. The crystalline precipitate, which formed on cooling, was twice recrystallized from acetic acid (in the presence of carbon); m. p. 147–148°. The yellow crystalline product was readily soluble on heating in acetic acid, methanol, ethanol, dioxane, and acetone. It showed a great tendency to form colloidal solutions.

Found %: S 14.66, 14.57; N 6.76, 6.58. Calc. for $C_7H_5O_5NS$: Calculated %: S 14.90; N 6.51.

The same product was obtained starting from 5-iodo- and 5-chlorofurylnitroethylenes.

b) The condensation of 2-formylfuran-5-ylthiocarboxylic acid (III) with nitromethane. A solution of 0.3 g of III and 0.03 g of NaOH in 10 ml of methanol was cooled in ice and salt and treated with a mixture of 0.04 g of CH_3NO_2 and 0.003 g of NaOH in 5 ml of water. The mixture was stirred and cooled for 1 hr until a homogeneous solution was obtained. This was then poured into 3 ml of 5% hydrochloric acid to give a dark yellow crystalline precipitate; m. p. 149–150° (from 60% alcohol). This gave no melting point depression when mixed with a sample of II.

SUMMARY

1. It has been shown that replacement of halogen in 5-halogenofurylnitroethylenes (chlorine, bromine, and iodine) by interaction with the thiocyanates of potassium or sodium only occurs in the presence of such catalysts as cobalt or copper salts. The products, depending on the solvent, are the previously undescribed 5-thiocyanatofurylnitroethylene or 2-(β -nitrovinyl)furan-5-ylthiocarboxylic acid.

2. The latter is also formed by condensation of nitromethane with 2-formylfuran-5-ylthiocarboxylic acid.

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* Original Russian pagination. See C. B. translation.

DERIVATIVES OF 7-AZAINDOLE

I. A NEW TYPE OF CLOSURE OF THE PYRROLINE RING

BY REACTION OF TRICHLOROCOLLIDINE

WITH SECONDARY AMINES

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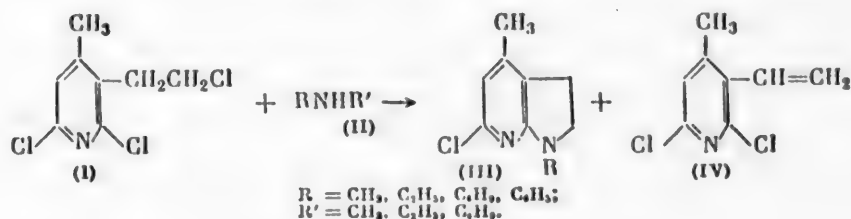
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The pyridinic analog of indole—7-azaindole—was first isolated from the lipidine fraction of bituminous coal tar [1]. Later synthetic investigations in the 7-azaindole series led to preparation of analogs of some biologically active indole derivatives: 7-azatryptophan, 7-azaheteroauxin, etc. [2] 7-Aza analogs of indigoid dyes were synthesized somewhat earlier [3]. Starting compounds for all these syntheses were 2-aminopyridines containing carboxyl or alkyl in the 3 position [2-4]. Hydrogenation of 7-azaindole derivatives has been described [1, 5] with the aim of preparing derivatives of 7-azaindoline. However the hydrogenation of 7-azaindole over nickel and copper-chromium catalysts only goes at high temperature (200°) and pressures above 100 atm, and leads to low yields of 7-azaindolines. Hexahydro derivatives of 7-azaindole are formed in presence of platinum catalyst.

In the present communication we describe a new route to derivatives of 7-azaindoline containing substituents in the pyridine ring.

In a study of transformations of 3,4-disubstituted 2,6-dihalopyridines we established that reaction of trichlorocollidine (I) with secondary aliphatic and aliphatic-aromatic amines (II) leads to formation not of N-disubstituted 2,6-dichloro-3-(β -aminoethyl)-4-methylpyridines but of 1-substituted 4-methyl-6-chloro-7-azaindolines (III). In nearly all cases 2,6-dichloro-3-vinyl-4-methylpyridine (IV) is formed at the same time.

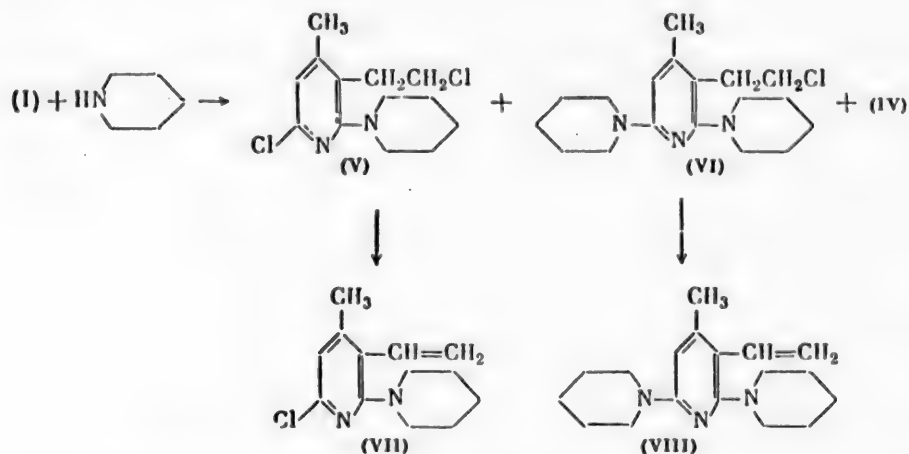


Secondary amines used in this reaction were dimethylamine, diethylamine, dibutylamine and N-methyl-aniline. It was found that the facility with which the reaction proceeds depends on the nature of the substituents at the nitrogen of the secondary amine. Reaction of trichlorocollidine with dimethylamine starts even at 80° whereas the same reaction with diethylamine does not go at below 120°, and that with N-methylaniline only starts at above 140°. In general, increase in chain length of alkyl radicals at the nitrogen, other conditions being the same, lowers the yield of 7-azaindoline derivative. Results of experiments on study of the influence of nature of substituents at the nitrogen of the secondary amine and of the reaction temperature on the process in question are set forth in the table.

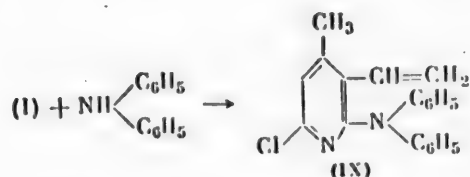
Secondary amine* (II)	Temperature	Yield (in %)		
		(III)	(IV)	(I)
$C_6H_5NHCH_3$	190°	91	—	—
$C_6H_5NHCH_3$	140	—	—	91.5
$(n-C_4H_9)_2NH$ **	140	17	29	43
$(C_2H_5)_2NH$	140	23	54	15
$(C_2H_5)_2NH$	120	12	35	45.5
$(C_2H_5)_2NH$	100	—	—	98
$(CH_3)_2NH$	140	54.5	13	31
$(CH_3)_2NH$	100	32.4	***	***
$(CH_3)_2NH$	80	5.5	***	***

Formation of 1-substituted 7-azaindolines by reaction of trichlorocollidine with secondary amines can be considered to proceed with replacement of one halogen atom in trichlorocollidine by the residue of the secondary amine with subsequent cleavage of alkyl halide and closure of the pyrroline ring. If a cyclic secondary amine, such as piperidine, is used, this mechanism enables the reaction to be interrupted at the first step since detachment of alkyl halide from the tertiary amine formed by reaction of (I) with secondary amine is excluded. Study of the structure of the resulting compounds can reveal whether a chlorine atom is replaced by the residue of the secondary amine in the pyridine ring or in the β -chloroethyl group of (I).

Reaction of trichlorocollidine with piperidine actually gave (apart from 2,6-dichloro-3-vinyl-4-methylpyridine) only products of substitution of one and two chlorine atoms in (I) by the piperidine residue. Chlorine atoms in the pyridine nucleus were replaced but the chlorine of the β -chloroethyl group was not. This was confirmed by transformation of the resulting compounds (V and VI) into the corresponding 2,6-disubstituted 3-vinyl-4-methylpyridines (VII and VIII) on treatment with alcoholic sodium hydroxide.



Certain features characterize the interaction of trichlorocollidine with diphenylamine. In this case the reaction starts at a temperature above 300° and leads to formation of only 2-diphenylamino-3-vinyl-4-methyl-6-chloropyridine (IX), evidently due to the difficulty of detachment of the chlorobenzene and in turn of closure of the pyrroline ring. Formation of a vinyl group by dehydrohalation is probably a secondary process which proceeds at high temperature.



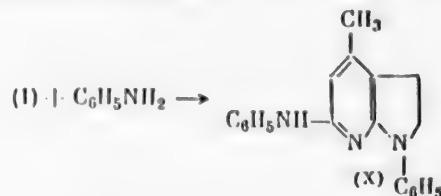
* In all experiments 2 moles of amine (II) were taken per mole of trichlorocollidine (I).

** In this case 2-(*n*-dibutylamino)-3-(β -chloroethyl)-4-methyl-6-chloropyridine (XI) was also isolated in 9% yield.

*** Yields of (I) and (IV) in these experiments are omitted.

On the basis of the above data we may conclude that the first step in the reaction of trichlorocollidine with secondary amines is replacement of the chlorine atom in the 2 position by the secondary amine residue. The mechanism of the further course of the reaction is now being investigated and will be the subject of the next communication. A study will also be made later of the position of the functional groups in compounds (V), (VII), (IX) and (XI) for which in the present communication we postulate the formula of 6-chloro-substituted pyridines as being the most probable.

Reaction of trichlorocollidine with aniline in place of secondary amines led to formation of 1-phenyl-4-methyl-6-phenylamino-7-azaindoline (X) in 88% yield.



In this case, just as in the previously described reaction of ethyl 2,6-dichloro-4-methylnicotinate with hydrazine hydrate [6], the process cannot be stopped at the stage of replacement of only one chlorine atom in the pyridine nucleus. Decrease in the quantity of aniline brought into reaction leads to a fall in the yield of (X) and to an increase in the quantity of unreacted trichlorocollidine.

EXPERIMENTAL

Reaction of trichlorocollidine with dimethylamine. A mixture of 4.5 g of trichlorocollidine and 7.5 ml of 24.3% solution of dimethylamine in chlorobenzene was heated in a sealed tube at 140° for 7 hr. Crystals of dimethylamine hydrochloride started to come down from the reaction mass during the heating. The reaction mixture was treated with 20 ml of water and extracted with ether. The ether-chlorobenzene solution was extracted with 20 ml of 15% hydrochloric acid and then twice with water (5 ml each time), and dried with potassium carbonate. The organic solvents were taken off in vacuo, and the residue was distilled at 14 mm. Two fractions were collected: 1st, b. p. 140–143°, 0.5 g; 2nd, b. p. 174–177°, 1.4 g.

The first fraction was a colorless, mobile liquid, readily soluble in common organic solvents and insoluble in water. It gave a positive reaction for the double bond with potassium permanganate and bromine and did not form a hydrochloride, picrate, or methiodide; n_D^{20} 1.5712. The compound was identified as 2,6-dichloro-3-vinyl-4-methylpyridine (IV) [7]. Yield 13%.

The second fraction crystallized on standing. Colorless crystals with m. p. 69–70°. Identified as trichlorocollidine [8]. No melting point depression in a mixed test. Yield 31%.

The hydrochloric acid solution obtained during extraction was made alkaline to phenolphthalein with 50% potassium carbonate solution and extracted with ether. After removal of the ether, the residue was distilled in vacuo and gave 2 g (54.5%) of 1,4-dimethyl-6-chloro-7-azaindoline with b. p. 149–150° (9 mm). The compound crystallized when rubbed with a rod. Colorless crystals with m. p. 66°. Readily soluble in common organic solvents, insoluble in water.

Found %: C 59.13, 59.36; H 6.09, 6.13; N 15.19; Cl 19.50. $C_9H_{11}N_2Cl$. Calculated %: C 59.18; H 6.02; N 15.34; Cl 19.46.

Hydrochloride. Colorless crystals with m. p. 192–193°. Readily soluble in alcohols and chloroform, insoluble in ether, benzene and acetone; hydrolyzed by water.

Found %: C 49.47, 49.60; H 5.46, 5.54; N 12.68; Cl 32.51. $C_9H_{11}N_2Cl \cdot HCl$. Calculated %: C 49.31; H 5.48; N 12.78; Cl 32.42.

Reaction of trichlorocollidine with diethylamine. A mixture of 4.5 g of trichlorocollidine and 3 g of diethylamine was heated in a sealed tube at 140° for 7 hr, and the product was worked up as above. There was obtained 2.05 g (5.4%) of 2,6-dichloro-3-vinyl-4-methylpyridine, 0.6 g (15%) of trichlorocollidine, and 0.9 g (23%) of 1-ethyl-4-methyl-6-chloro-7-azaindoline.

Colorless, oily liquid, easily soluble in common organic solvents, insoluble in water; b. p. 157–158° (7 mm), n_D^{20} 1.5660.

Found %: C 61.37; H 6.85; N 14.06, 13.96; Cl 18.25, 18.25. $C_{10}H_{13}N_2Cl$. Calculated %: C 61.07; H 6.62; N 14.24; Cl 18.06.

Hydrochloride. Colorless crystals, m. p. 136–137° (from acetone). Readily soluble in ether, benzene and acetone; hydrolyzed by water.

Found %: N 11.98, 11.89; Cl' 15.34. $C_{10}H_{13}N_2Cl \cdot HCl$. Calculated %: N 12.01; Cl' 15.24.

Reaction of trichlorocollidine with n-dibutylamine. A mixture of 8.96 g of trichlorocollidine and 9.68 g of n-dibutylamine was heated at 140° for 7 hr. The reaction mass was treated with 20 ml of water and extracted with ether. The ethereal solution was extracted with 30 ml of 15% hydrochloric acid, then twice with water (10 ml each time), and dried with potassium carbonate. The ether was driven off and the residue distilled in vacuo to give the following fractions: 1st, b. p. 140–143° (14 mm)–2,6-dichloro-3-vinyl-4-methylpyridine; yield 2.25 g (29%); 2nd, b. p. 174–177° (14 mm)–trichlorocollidine; yield 3.9 g (43%); 3rd, b. p. 175° (1 mm). The product was a colorless viscous, oily liquid, readily soluble in common organic solvents, insoluble in water; soluble in concentrated hydrochloric acid with formation of a hydrochloride which was very easily hydrolyzed on dilution with water. Judging by the analysis, the compound appears to be 2-(n-dibutylamino)-3-(8-chloroethyl)-4-methyl-6-chloropyridine. Yield 0.8 g (9%).

Found %: C 60.48, 60.83; H 8.19, 8.47; N 8.58, 8.87; Cl 22.55, 22.51. $C_{16}H_{26}N_2Cl_2$. Calculated %: C 60.56; H 8.20; N 8.83; Cl 22.40.

The hydrochloric acid solution obtained during the extraction was made alkaline to phenolphthalein with 50% potassium carbonate solution. An oil separated out and was extracted with ether. After the ether had been driven off, the residue was distilled in vacuo to give 1.5 g (17%) of 1-n-butyl-4-methyl-6-chloro-7-azaindoline. A colorless oil, readily soluble in common organic solvents, poorly soluble in water. B. p. 147–148° (1 mm), n_D^{19} 1.5507.

Found %: C 64.12, 64.32; H 7.79, 7.46; N 12.45, 12.73; Cl 15.67, 15.64. $C_{12}H_{17}N_2Cl$. Calculated %: C 64.14; H 7.57; N 12.48; Cl 15.81.

Reaction of trichlorocollidine with N-methylaniline. A mixture of 8.96 g of trichlorocollidine and 8.56 g of N-methylaniline was heated at 190° for 7 hr. The resulting viscous, glassy mass was insoluble in ether. To the reaction mass was added 20 ml of water, and extraction was effected with chloroform. The chloroform solution was dried with potassium carbonate, evaporated in vacuo, and distilled. A fraction with b. p. 238–240° (5 mm) was collected. Yield of 1-phenyl-4-methyl-6-chloro-7-azaindoline 8.9 g (91%). The substance crystallized on standing. Colorless crystals with m. p. 116.5–117° (from benzene). Readily soluble in alcohols, chloroform and acetone, poorly in benzene and ether, insoluble in water and ligroine.

Found %: C 68.91; H 5.24; N 11.54, 11.62; Cl 14.80, 14.85. $C_{14}H_{13}N_2Cl$. Calculated %: C 68.71; H 5.32; N 11.45; Cl 14.52.

1-Phenyl-4-methyl-6-phenylamino-7-azaindoline (X). 1) A mixture of 4.5 g of trichlorocollidine and 7.5 g of aniline was heated at 190° for 7 hr. During the reaction aniline hydrochloride sublimed (2.8 g with m. p. 197–198° came over) [9]. The reaction mass was treated with 50 ml of anhydrous alcohol. The hydrochloride of (X) came down (5.15 g). The mother liquor was evaporated in vacuo. The residue (4 g) was treated with 30 ml of anhydrous chloroform. The precipitated aniline hydrochloride (2.3 g, m. p. 197–198°) was filtered, the chloroform was distilled, and the residue triturated with 10 ml of absolute alcohol. In this way a further 0.8 g of hydrochloride of (X) was obtained. Total yield 5.95 g (88.1%). Light-yellow crystals. Readily soluble in chloroform, insoluble in alcohol, acetone, ether, benzene and water. M. p. 210–211°.

Found %: C 71.40, 71.31; H 5.97, 5.94; N 12.25, 12.34; Cl 10.56, 10.45. $C_{20}H_{19}N_3 \cdot HCl$. Calculated %: C 71.11; H 5.92; N 12.44; Cl 10.52.

The base forms colorless crystals. Readily soluble in ether, alcohols, chloroform, acetone and benzene, insoluble in water and ligroine. Negative Beilstein reaction for chlorine. M. p. 97–98° (from ligroine).

Found %: C 79.64, 79.72; H 6.40, 6.37; N 13.96, 13.72. $C_{20}H_{19}N_3$. Calculated %: C 79.73; H 6.31; N 13.95.

2) A mixture of 4.5 g of trichlorocollidine and 3.72 g of aniline was heated at 190° for 7 hr. During the reaction 1.7 g of aniline hydrochloride sublimed. The reaction mass was dissolved in 50 ml of chloroform. The chloroform solution was washed first with water (two lots of 50 ml each), then with 50 ml of 50% potassium carbonate solution; it was then dried with potassium carbonate and evaporated in vacuo. The residue was dissolved in 20 ml of anhydrous alcohol and treated with alcoholic hydrogen chloride until acid to Congo. Light-yellow crystals of the hydrochloride of (X) came down. Yield 3.85 g (58.6%), m. p. 210–211°. The alcoholic mother liquor was evaporated in vacuo and the residue distilled. A fraction with b. p. 173–177° (14 mm) was collected. Trichlorocollidine crystallized on standing; m. p. 70°, 1.4 g (31%). No melting point depression in a mixed test.

Reaction of trichlorocollidine with piperidine. A mixture of 8.96 g of trichlorocollidine and 6.4 g of piperidine was heated at 110° for 7 hr. The reaction mass was treated with 20 ml of water and extracted with ether. The ethereal solution was extracted with 30 ml of 15% hydrochloric acid, then twice with water (10 ml each time), and dried with potassium carbonate. The ether was driven off and the residue distilled in vacuo to give the following fractions: 1st, b. p. 140–143° (14 mm), 2,6-dichloro-3-vinyl-4-methylpyridine, 1.8 g (23.2%); 2nd, b. p. 173–177° (14 mm), trichlorocollidine, 3.1 g (34.6%); 3rd, b. p. 154° (1 mm), a colorless, viscous oil, readily soluble in common organic solvents, insoluble in water, soluble in concentrated hydrochloric acid with formation of a hydrochloride which was very easily hydrolyzed when diluted with water. The analytical data indicated that the substance was 2-(N-piperidyl)-3-(β-chloroethyl)-4-methyl-6-chloropyridine (V). Yield 2.3 g (21%).

Found %: C 57.31, 57.36; H 6.50, 6.48; N 10.25; Cl 26.02, 26.06. $C_{13}H_{13}N_2Cl_2$. Calculated %: C 57.14; H 6.59; N 10.25; Cl 26.01.

The hydrochloric acid solution obtained during extraction was made alkaline to phenolphthalein with 50% potassium carbonate solution and extracted with ether. After the ether had been driven off, the residue was distilled in vacuo to give 2.2 g (18.2%) of 2,6-bis-(N-piperidino)-3-(β-chloroethyl)-4-methylpyridine (VI). A viscous, yellowish oil, readily soluble in common organic solvents, insoluble in water. B. p. 207–209° (11 mm), n_D^{20} 1.5568.

Found %: C 67.20; H 8.69; N 13.08; Cl 11.15, 11.18. $C_{18}H_{23}N_3Cl$. Calculated %: C 67.18; H 8.71; N 13.06; Cl 11.04.

2,6-Bis-(N-piperidino)-3-vinyl-4-methylpyridine (VIII). A solution of 0.5 g of 2,6-bis-(N-piperidino)-3-(β-chloroethyl)-4-methylpyridine and 0.03 g of sodium hydroxide in 5 ml of anhydrous alcohol was boiled for 8 hr. The precipitated sodium chloride (0.07 g) was filtered off. The alcoholic solution was evaporated and the residue distilled in vacuo (0.8 mm) at 185–186°. Yield of (VIII) 0.43 g (93%). A colorless, oily substance, readily soluble in ordinary organic solvents, insoluble in water. The product gives a positive reaction for the double bond with potassium permanganate and with bromine, and a negative Beilstein reaction for chlorine; n_D^{20} 1.5554.

Found %: C 75.74, 75.72; H 9.29, 9.37; N 14.67, 14.69. $C_{18}H_{27}N_3$. Calculated %: C 75.79; H 9.48; N 14.73.

2-(N-Piperidino)-3-vinyl-4-methyl-6-chloropyridine (VII). A mixture of 0.5 g of 2-(N-piperidino)-3-(β-chloroethyl)-4-methyl-6-chloropyridine (V) and 0.08 g of sodium hydroxide was boiled in 5 ml of absolute alcohol. The precipitated sodium chloride was filtered off (0.05 g). The alcoholic filtrate was evaporated and the residue distilled in vacuo to give 0.4 g (92.4%) of 2-(N-piperidino)-3-vinyl-4-methyl-6-chloropyridine (VII) with b. p. 108–110° (1 mm). A colorless oil, readily soluble in common organic solvents, insoluble in water; dissolves in concentrated hydrochloric acid with formation of a hydrochloride which easily hydrolyzes when water is added. Gives a positive reaction for the double bond with potassium permanganate and with bromine; n_D^{20} 1.5836.

Found %: C 66.29, 66.27; H 6.97, 7.07; N 11.73, 11.61; Cl 14.92, 15.02. $C_{13}H_{17}N_2Cl$. Calculated %: C 65.94; H 7.19; N 11.84; Cl 15.01.

Reaction of trichlorocollidine with diphenylamine. Trichlorocollidine (5.6 g) and diphenylamine (8.6 g) were heated at 310° for 12 hr. The mass darkened during reaction and 6.9 g of diphenylamine hydrochloride distilled over, m. p. 180° (decomp.) [10] (no melting point depression in a mixed test with diphenylamine).

hydrochloride). The reaction mass was dissolved in 20 ml of chloroform. The solution was washed twice with 17% hydrochloric acid (10 ml each time) and dried with potassium carbonate. After the chloroform had been distilled off, the residue was distilled in vacuo and the following fractions were collected:

First fraction: b. p. 173–177° (14 mm), 3.7 g. The substance crystallized, m. p. 30–35°. The crystals were deliquescent in air. For separation of diphenylamine, the first fraction was dissolved in 30 ml of anhydrous ether and treated with gaseous hydrogen chloride until it had an acidic reaction to Congo. Diphenylamine hydrochloride (1 g) came down and was separated. The remaining ethereal solution was evaporated in vacuo to give 2.7 g (48%) of trichlorocollidine with m. p. 68–69°. No depression in a mixed melting test with trichlorocollidine.

Second fraction: b. p. 220–221° (0.5 mm). The substance crystallized when triturated with ether. Yield of 2-diphenylamino-3-vinyl-4-methyl-6-chloropyridine (IX) 2.05 g (25%). Colorless crystals, readily soluble in alcohols, acetone, and chloroform, poorly in benzene and ether, insoluble in water; m. p. 182–183°.

Found %: C 74.59, 74.97; H 5.28, 5.19; N 8.96, 8.68; Cl 10.99, 10.98. $C_{20}H_{17}N_2Cl$. Calculated %: C 74.88; H 5.30; N 8.73; Cl 11.08.

SUMMARY

1. A new type of pyrroline ring closure involves reaction of trichlorocollidine with secondary amines. The effect of temperature and of substituents in the secondary amine on the reaction course is studied.
2. It is shown that the first step in the reaction is replacement of the chlorine in the 2 position by the secondary amine residue. Closure of the pyrroline ring then occurs with total removal of alkyl halide.
3. A preparative method of synthesis of previously undescribed derivatives of 7-azaindoline substituted in the pyridine ring is proposed.

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BICYCLIC COMPOUNDS ON THE BASIS OF 2,6-LUTIDINE

IV. 3-SUBSTITUTED 9-METHYL-3,9-DIAZABICYCLO-(3,3,1)-NONANES

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In the preceding communications we described derivatives of 3,9-oxabicyclo-(3,3,1)-nonane [1] possessing pharmacological activity. It was to be expected that similar derivatives of the related bicyclic compound 3,9-diazabicyclo-(3,3,1)-nonane



would not be less interesting from the pharmacological aspect. Compounds of this series have hardly been studied. One paper only [2] has been published; this describes the preparation and properties of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane dihydrochloride.

We made use of this method and introduced some modifications which simplified the synthesis and increased the yields at some steps.

The dimethyl N-methyldipiecolinate (I) was prepared by our earlier method for the corresponding diethyl ester [3].

The benzylimide of N-methyldipiecolinic acid (II) was prepared by reaction of (I) with benzylamine. During this reaction methyl alcohol is formed and seriously lowers the boiling point of the reaction mass. By distilling off the methyl alcohol we were able to cut down the reaction period from 48 hr, reported in the literature, to 5 hr and at the same time to increase the yield.

According to the literature the reduction of compound (II) by lithium aluminum hydride in an ethereal medium requires a period of 72 hr. Employment of an ether-benzene mixture in place of ether enabled us to cut down the reaction period to 20 hr without serious effect on the yield. The resulting 3-benzyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (III) was reduced by hydrogen in presence of palladium chloride to 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (IV).

A series of 3-substituted derivatives was prepared from compound (IV). Methylation of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane with a mixture of formic acid and formalin gave 3,9-dimethyl-3,9-diazabicyclo-(3,3,1)-nonane (V). This compound gives a quaternary salt only with one mole of methyl iodide—indicating that the basicities of the two nitrogen atoms are not identical.

Sulfonation with the help of pyridine sulfotrioxide in an aqueous medium in the cold and in a dichloroethane medium with heating in a sealed tube leads to the N-sulfonic acid (VI) which was isolated as the potassium and barium salts.

The corresponding amides of substituted aminoacids (VII, Table 1) were obtained by reaction of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane with β -chloropropionyl chloride, α -bromopropionyl chloride and chloroacetyl chloride in an aqueous alkaline medium or in anhydrous benzene, with subsequent treatment of the reaction products with dimethylamine, diethylamine, piperidine and morpholine.

TABLE 1

3-Dialkylamino- (or piperidino- or morpholino)-acyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes

Compound number	Formula	Boiling point (pressure in mm)	Yield (%)	% C		% H		% N		% Cl		% I	
				cal- culated	found	cal- culated	found	cal- culated	found	cal- culated	found	cal- culated	found
VIIa•	$C_{13}H_{25}ON_3$	133–135° (0.3)	68.9	—	—	—	—	17.57	17.14	—	—	—	—
VIIb•	$C_{13}H_{29}ON_3$	148–150 (0.25)	72.0	67.41	67.54	10.86	11.02	15.73	15.59	—	—	—	—
	$C_{13}H_{29}ON_3 \cdot 2CH_3I$	M. P. 231–232	—	—	—	—	—	7.62	7.74	—	—	46.09	45.83
VIIc•	$C_{10}H_{29}ON_3$	170 (0.25)	65.9	—	—	—	—	—	—	—	—	—	—
	$C_{16}H_{29}ON_3 \cdot 2HCl$	M. P. 216–218	—	—	—	—	—	11.93	11.61	20.17	19.79	—	—
VIId•	$C_{15}H_{27}O_2N_3$	170–172 (0.3)	66.0	64.05	64.48	9.60	9.69	14.94	15.02	—	—	—	—
	$C_{15}H_{27}O_2N_3 \cdot 2HCl$	M. P. 238–240	—	—	—	—	—	11.86	11.88	20.05	19.93	—	—
VIIe••	$C_{14}H_{25}O_2N_3$	157–159 (0.25)	48.5	62.92	63.11	9.36	9.66	15.73	15.80	—	—	—	—
VIIf••	$C_{13}H_{27}O_2N_3$	163–165 (0.3)	42.7	64.05	63.59	9.61	9.58	14.94	14.86	—	—	—	—
	$C_{15}H_{27}O_2N_3 \cdot 2HCl$	M. P. 265–267	—	—	—	—	—	11.86	11.76	20.05	20.28	—	—

• Prepared by method a).

•• Prepared by method b).

TABLE 2

3-Dialkylamino- (or piperidino- or morpholino-) alkyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes

Compound number	Formula	Boiling point (pressure in mm)	Yield (%)	% C		% H		% N		% I	
				calculated	found	calculated	found	calculated	found	calculated	found
VIIIa	$C_{13}H_{27}N_3 \cdot 2CH_3I$	94-96° (0.35) M. p. 255-257	75	69.33	69.10	12.00	12.02	8.25	8.14	43.90	43.84
VIIIb	$C_{13}H_{27}N_3 \cdot 2CH_3I$	113-115° (0.3) M. p. 244-245	76.5	71.14	71.11	12.25	12.18	7.82	7.68	47.29	46.83
VIIIc	$C_{13}H_{27}N_3 \cdot 2CH_3I$	133-135° (0.35) M. p. 258-260	76	72.45	72.73	11.70	11.90	15.84	15.89	46.26	45.87
VIIId	$C_{15}H_{29}ON_3 \cdot 2CH_3I$	127-130° (0.3) M. p. 244-245	72.3	—	—	—	—	15.73	15.52	46.09	45.90
VIIIf	$C_{14}H_{27}ON_3 \cdot 2CH_3I$	118-130° (0.4) M. p. 235-237	66.0	66.40	66.44	10.66	10.65	16.00	16.36	47.30	47.23
VIIIe	$C_{15}H_{29}ON_3 \cdot 2CH_3I$	123-125° (0.3) M. p. 212-214	50.0	67.41	66.97	10.86	10.92	15.73	15.70	46.09	46.09

Reaction of 3-(ω -hydroxyalkyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes with benzoyl chloride, p-nitrobenzoyl chloride and p-bromobenzoyl chloride gave the corresponding esters (XII, Table 3).

Reaction of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane dihydrochloride with succinyl, glutaryl, and adipyl chlorides in an aqueous alkaline medium gave the corresponding diamides (XIII, Table 4). Reduction of the latter with lithium aluminum hydride gave the diamines which formed diquaternary salts with methyl iodide (XIV, Table 5).

Pharmacological tests on the new compounds, carried out in the department of pharmacology by B. A. Medvedev, showed that derivatives of 3,9-diazabicyclo-(3,3,1)-nonane are more active than corresponding derivatives of 3,9-oxabicyclo-(3,3,1)-nonane.

The most interesting of the compounds studied is 1,4-bis-[9-methyl-3,9-diazabicyclo-(3,3,1)-nonano-3]-butane methiodide (XIVa), which has a strong curarelike activity nearly equal to that of decamethonium iodide.

EXPERIMENTAL

N-Methyldiisopicolinic acid benzylimide

(II). A mixture of 7 g of dimethyl N-methyldiisopicolinate and 5.7 g of benzylamine was refluxed for 4 hr, during which operation the boiling point of the reaction mass fell from 170-180° down to 115-120°. The reflux condenser was replaced by a sloping one and the methyl alcohol formed (1.5-2 ml) was distilled off. The reflux condenser was again put in position and the reaction mass boiled for another hour. After addition of 25 ml of ligroine to the slightly cooled mass, boiling was resumed for 10 min, and the ligroine layer was decanted. The operation was twice repeated. The precipitate was filtered from the cooled ligroine solution and recrystallized from ligroine. There was obtained 5.67 g (67.5%) of white crystals with m. p. 113-115° [2].

3-Benzyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (III). N-Methyldiisopicolinic acid benzylimide (15.4 g) was reduced with lithium aluminum hydride (4.5 g) in ether-benzene solution for 20 hr. There was obtained 11.36 g (82.9%) of substance with b. p. 112-115° (0.3 mm) in the form of a colorless, oily liquid [2].

TABLE 3

3- γ -(δ)-Acyloxypropyl(butyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes

Compound number	Empirical formula	Melting point	Yield (%)	% N		% Cl	
				calculated	found	calculated	found
XIIa	$C_{18}H_{25}O_2N_2 \cdot 2HCl$	213–216°	94.0	7.46	7.42	18.93	18.62
XIIb	$C_{18}H_{25}O_4N_3 \cdot 2HCl$	202–204	77.6	10.00	9.72	16.90	16.36
XIIc	$C_{18}H_{25}O_2N_2Br \cdot 2HCl$	209–211	87.0	6.16	6.53	15.64	15.31
XIId	$C_{19}H_{28}O_2N_2 \cdot 2HCl \cdot H_2O$	72–75	87.0	6.88	6.82	17.77	17.43
XIIe	$C_{19}H_{27}O_4N_3 \cdot 2HCl$	200.5–202.5	87.0	9.67	9.32	16.35	15.97
XIIIf	$C_{19}H_{27}O_2N_2Br \cdot 2HCl$	210–211	79.8	5.98	6.03	15.17	15.04

Monomethiodide: white crystals with m. p. 258° [2].

Found %: I 34.19. $C_{18}H_{25}N_2I$. Calculated %: I 34.14.

9-Methyl-3,9-diazabicyclo-(3,3,1)-nonane (IV). 3-Benzyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (11 g) was dissolved in 300 ml of alcohol, the solution was made acid with excess of alcoholic hydrogen chloride, and the reaction mass reduced with hydrogen in presence of 3 g of palladium chloride under a pressure of 20–30 cm water column. After hydrogen had ceased being absorbed, the precipitate was filtered together with the catalyst and washed free of catalyst with hot water. The aqueous alcoholic mother liquors were evaporated to dryness and there was obtained 10.8 g (97.2%) of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane which crystallized with one molecule of water and melted at 258–260° [2].

Found %: Cl 30.83, 30.82. $C_8H_{18}N_2Cl_2 \cdot H_2O$. Calculated %: Cl 30.73.

The compound sublimes easily and loses water at the same time.

Found %: Cl 33.19, 33.04. $C_8H_{18}N_2Cl_2$. Calculated %: Cl 33.33.

The base, liberated from the dihydrochloride, is a volatile substance with b. p. 93° (15 mm), partially crystallizing at room temperature.

Found %: C 68.47; H 11.48. $C_8H_{16}N_2$. Calculated %: C 68.57; H 11.42.

3,9-Dimethyl-3,9-diazabicyclo-(3,3,1)-nonane (V). A mixture of 0.73 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane, 0.58 g of 33.5% formalin, and 0.72 g of formic acid was heated on a boiling water bath for 15 hr. After completion of the reaction, the mass was made alkaline with excess of 50% potassium carbonate solution and extracted with ether. The ethereal extract was dried, the ether driven off, and the residue distilled in vacuo to give 0.54 g (67.5%) of a colorless, mobile liquid with b. p. 69° (7 mm).

Found %: C 70.07; H 11.66; N 18.45. $C_9H_{18}N_2$. Calculated %: C 70.13; H 11.68; N 18.18.

Dihydrochloride: white crystals with m. p. 275–276°.

Found %: Cl 30.95. $C_9H_{20}N_2Cl_2$. Calculated %: Cl 31.27.

Monomethiodide: white crystals with m. p. 291°.

Found %: N 9.25; I 42.51. $C_{11}H_{24}N_2I_2$. Calculated %: N 9.45; I 42.90.

Sulfonation of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane with pyridine sulfotrioxide. a) Ice was added to a solution of 0.84 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in 4 ml of water, followed by 0.94 g of pyridine sulfotrioxide. The reaction mass was shaken for 15 min, 1.64 g of potassium carbonate was added, and shaking was continued with ice cooling for 30 min. Undissolved potassium carbonate was brought into solution by addition of water, and the solution was evaporated in a dish on a water bath. The dry residue was extracted with boiling anhydrous alcohol, and the alcoholic solution evaporated. There was obtained 1.46 g (88.4%) of

TABLE 4

Derivatives of Succinic, Glutaric, and Adipic Acids

Compound number	Empirical formula	Boiling point (pressure in mm)	Yield (%)	% C		% H		% N	
				calculated	found	calculated	found	calculated	found
XIIIa	$C_{20}H_{34}O_2N_4$	254–255° (0.4)	51.0	66.60	66.32	9.39	9.16	—	—
XIIIb	$C_{21}H_{36}O_2N_4$	255 (0.4)	63.0	67.02	67.00	9.57	9.78	14.89	14.84
XIIIc	$C_{22}H_{38}O_2N_4$	244 (0.5)	74.3	67.69	67.42	9.10	9.52	14.35	14.27

the potassium salt of 3-sulfo-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (VI) which was recrystallized from anhydrous alcohol. The potassium salt crystallizes with one molecule of water. Barium sulfate comes down when the potassium salt is heated in presence of barium chloride in hydrochloric acid.

Found %: Cl 34.78; H 6.15; N 10.14; S 11.59. $C_8H_{15}O_3N_2SK \cdot H_2O$. Calculated %: C 34.51; H 6.29; N 9.98; S 11.12.

b) A mixture of 1.35 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane, 4.61 g of pyridine sulfotrioxide, and 10.5 ml of dry dichloroethane (dried over phosphorus pentoxide) was heated in a sealed tube on a boiling water bath for 15 hr. At the end of the reaction the dichloroethane layer was poured off, and the residue dissolved in water. Unreacted pyridine sulfotrioxide was filtered off. The solution was treated with carbon, filtered, and heated to the boil. To the boiling solution was gradually added 7.81 g of $BaCO_3$ and boiling continued for 45 min. The $BaSO_4$ and excess $BaCO_3$ were filtered off, and the filtrate was again treated with carbon and evaporated. The operation was repeated three times. Absolute alcohol was then added, the mass stirred, and the resulting precipitate filtered and washed with absolute alcohol and ether. There was obtained 1.46 g (53.8%) of barium salt of 3-sulfo-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (VI).

Found %: N 9.73; S 11.13. $C_8H_{15}O_3N_2S_2Ba$. Calculated %: N 10.19; S 11.55.

3-Dialkylamino-(or piperidino- or morpholino)-acyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes (VII).

These compounds were prepared by the following methods: a) A solution of 5.48 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane dihydrochloride in 20 ml of water was cooled to 5° and simultaneous dropwise addition was made with stirring of 3.3 g of β -chloropropionyl chloride and a solution of 3.02 g of sodium hydroxide in 4 ml of water. After the additions, stirring was continued at the same temperature for another 30 min, after which the cooling and stirring were interrupted until the temperature of the mass rose to 16°. The mass was made alkaline with excess of 50% potassium carbonate solution and extracted with ether; the extract was dried with anhydrous sodium sulfate and the ether driven off. There was obtained 4.1 g (74%) of 3-(β -chloropropionyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in the form of a colorless oil. This was boiled for 5 hr with 20 ml of 20% alcoholic dimethylamine. The alcohol was then distilled off, the residue treated with 50% potassium carbonate solution, and the deposited oil extracted with ether. The solution was dried with anhydrous sodium sulfate and the ether distilled off. The residue was distilled in vacuo to give 2.93 g (68.9%) of 3-(β -dimethylaminopropionyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane with b. p. 133–135° (0.3 mm).

b) To a solution of 2.97 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in 15 ml of dry benzene (cooled with ice) was gradually added dropwise a solution of 2.39 g of monochloroacetyl chloride in 10 ml of dry benzene. After the addition, the reaction mass was stirred for another 1.5 hr with ice cooling and for 3 hr at room temperature. Thereupon it was diluted with 35 ml of anhydrous ether, and the precipitate filtered off. Yield 4.63 g (86%) of 3-chloroacetyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane hydrochloride. This was boiled with 6.36 g of morpholine in 30 ml of absolute alcohol for 5 hr. The alcohol was then distilled off and the residue worked up as described for method a). Yield 2.37 g (48.5%) of 3-(N-morpholinoacetyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in the form of an oily liquid with b. p. 157–159° (0.25 mm).

Data for the compounds are set forth in Table 1.

TABLE 5

 α, ω -Bis[9-methyl-3,9-diazabicyclo-(3,3,1)-nonano-3]-alkanes

Compound number	Empirical formula	Boiling point (pressure in mm)	Yield (%)	% C		% H		% N		% I	
				cal- culated	found	cal- culated	found	cal- culated	found	cal- culated	found
XIVa	$C_{20}H_{36}N_4 \cdot 2CH_3I$	178-180° (0.3) M. p. 261-263	77.0	—	—	—	—	—	—	—	—
XIVb	$C_{21}H_{40}N_4 \cdot 2CH_3I$	206-207° (0.5) M. p. 240-242	80.0	72.41	72.20	11.49	11.54	16.09	15.58	41.10	40.69
XIVc	$C_{22}H_{42}N_4 \cdot 2CH_3I$	175-177° (0.2) M. p. 244-244.5	75.4	72.92	72.24	11.60	11.31	8.86	9.03	39.31	39.68

3-Dialkylamino- (or piperidino- or morpholino-) -alkyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes (VIII). Compounds (VII) were reduced with lithium aluminum hydride in ethereal solution. Data for the products are given in Table 2.

3-Carboethoxyacetyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (IXa). Gradual, dropwise addition of a solution of 4.36 g of carboethoxyacetyl chloride in 10 ml of dry benzene was made to an ice-cooled solution of 4.05 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in a mixture of 15 ml of dry benzene and 10 ml of absolute ether. The 3-carboethoxyacetyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane monohydrochloride formed during the reaction came down in the form of a yellow, oily precipitate. After completion of addition of the carboethoxyacetyl chloride, 25 ml of absolute ether was added and stirring was continued for another hour. During this operation the oily precipitate changed into a cream-colored, hygroscopic powder. Into the reaction mass was stirred an excess of 50% potassium carbonate solution with shaking. The ether-benzene layer was separated and the aqueous layer further extracted with ether. The combined extracts were dried with anhydrous sodium sulfate, the solvent distilled off, and the residue distilled in vacuo to give 0.65 g of starting substance (IV), with b. p. 93-95° (15 mm), and 3.53 g (48%) of a substance with b. p. 153-155 (0.3 mm) whose analysis corresponded to 3-carboethoxyacetyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane.

Found %: N 11.04, 11.07. $C_{13}H_{22}O_3N_2$. Calculated %: N 11.02.

3-(β -Carbomethoxypropionyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (IXb). Reaction of 3.62 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane with 3.89 g of β -carbomethoxypropionyl chloride by the above procedure gave 4.05 g (61.7%) of 3-(β -carbomethoxypropionyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane with b. p. 152-153° (0.3 mm) and 0.56 g of the original compound (IV).

Found %: N 10.78, 10.69. $C_{13}H_{22}O_3N_2$. Calculated %: N 11.02.

3-(γ -Hydroxypropyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (Xa). 3-Carboethoxyacetyl-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (2.37 g) was reduced with 1 g of lithium aluminum hydride in ether-benzene solution. There was obtained 1.55 g (84 %) of substance with b. p. 118-120° (0.4 mm) in the form of a colorless, oily liquid.

Found %: N 13.99, 13.99. $C_{11}H_{22}ON_2$. Calculated %: N 14.14.

3-(δ -Hydroxybutyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (Xb). 3-(β -Carbomethoxypropionyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (3.25 g) was reduced by lithium aluminum hydride (1.5 g) in ether-benzene solution. There was obtained 2.31 g (85 %) of substance with b. p. 128-130° (0.35 mm).

Found %: C 67.16; H 11.58; N 13.26. $C_{12}H_{24}ON_2$. Calculated %: C 67.92; H 11.32; N 13.20.

3-(γ -Chloropropyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (XIa). A solution of 2.3 g of 3-(γ -hydroxypropyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in 7 ml of anhydrous alcohol was acidified with alcoholic hydrogen chloride until acid to Congo. The solution was then evaporated in vacuo. To the caramel-like residue were added 15 ml of dry chloroform and 25 ml of thionyl chloride, and the reaction mass was heated for an hour at 75°. It was then evaporated to dryness in vacuo. The residue was treated with 50% potassium carbonate solution and extracted with ether. Drying of the extract with anhydrous sodium sulfate and distillation of the solvent gave 1.85 g (73.7%) of a colorless, mobile liquid with b. p. 95–97° (0.4 mm). On standing the substance changed into a treacly mass, readily soluble in water. It was evidently an internal quaternary salt.

Found %: N 12.72; Cl 16.15. $C_{11}H_{21}N_2Cl$. Calculated %: N 12.93; Cl 16.39.

Dihydrochloride: a white, hygroscopic powder.

3-(δ -Chlorobutyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane (XIb). The above method was used for the preparation, from 3.23 g of 3-(δ -hydroxybutyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane, of 2.85 g (81%) of 3-(δ -chlorobutyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in the form of a readily mobile, colorless liquid with b. p. 115–117° (0.55 mm).

Found %: N 12.58; Cl 15.49. $C_{12}H_{23}N_2Cl$. Calculated %: N 12.14; Cl 15.40.

On standing the compound forms an internal quaternary salt in the form of a brown, treacly mass.

Dihydrochloride: colorless, very hygroscopic crystals.

3- γ -(δ)-Acloxypropyl (butyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonanes (XII). A mixture of 0.7 g of 3-(γ -hydroxypropyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane and 0.75 g of benzoyl chloride was heated at the boil in 15 ml of dry benzene for 3 hr. The reaction mass was then acidified (to Congo) with alcoholic hydrogen chloride, 20 ml of absolute ether was added, and the white precipitate was filtered and thoroughly washed with ether. There was obtained 1.24 g (94%) of 3-(γ -benzoyloxypropyl)-9-methyl-3,9-diazabicyclo-(3,3,1)-nonane in the form of white crystals with m. p. 213–216°. After crystallization from absolute alcohol the compound melted at 215–216°. Esters prepared by this method are set forth in Table 3.

Succinyl-bis-[3-[9-methyl-3,9-diazabicyclo-(3,3,1)-nonane]] (XIIIa). Into a solution of 10 g of 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane dihydrochloride in 25 ml of water was stirred a solution of 3.35 g of sodium hydroxide in 10 ml of water, and the reaction mass was cooled to -5°. At this temperature dropwise addition was simultaneously made of 3.7 g of succinyl dichloride and a solution of 1.7 g of sodium hydroxide in 5 ml of water. This step was followed by addition to the reaction mass of 15 ml of 50% potassium carbonate solution. An oil separated and was extracted with chloroform. The extract was dried with anhydrous sodium sulfate, the chloroform taken off, and the residue distilled in vacuo to give 4 g (51%) of a treacly, light-yellow mass with b. p. 254–255° (0.4 mm).

Derivatives of glutaric and adipic acids were prepared in similar fashion (Table 4).

α,ω -Bis[9-methyl-3,9-diazabicyclo-(3,3,1)-nonano-3]-alkanes (XIV). These compounds were prepared by reduction of the corresponding diamides (XIII) with lithium aluminum hydride in ether-benzene solution. Data are set forth in Table 5.

SUMMARY

1. Syntheses were effected of derivatives of 3,9-diazabicyclo-(3,3,1)-nonane containing a methyl group in the 9 position and various substituents - acyl, alkyl, hydroxy, carboxy, aminoalkyl, etc. - in the 3 position.
2. 3,9-Dimethyl-3,9-diazabicyclo-(3,3,1)-nonane was found to form only a monomethiodide with methyl iodide, the latter combining in the 9 position of the bicycle. This showed that the nitrogen in the 9 position is more basic than that in the 3 position.
3. Bis [9-methyl-3,9-diazabicyclo-(3,3,1)-nonano-3]-alkanes and their derivatives were prepared from 9-methyl-3,9-diazabicyclo-(3,3,1)-nonane.

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SYNTHESIS AND CATALYTIC TRANSFORMATIONS OF
 α -DECYLTHIOPHANE OVER ALUMINOSILICATE
 CATALYST

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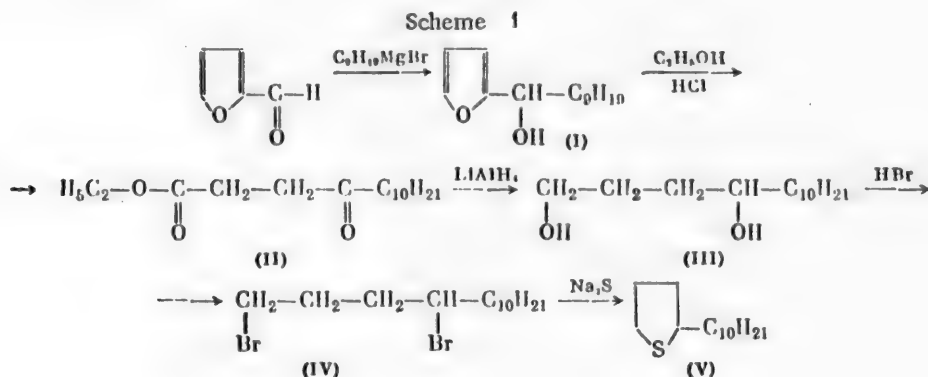
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In the present work we submit data for the synthesis and catalytic transformations over aluminosilicate catalyst of α -decylthiophane, a compound not previously described in the literature. We prepared this sulfide by the general method of synthesis of α -alkylthiophanes proposed by R. D. Obolentsov and V. G. Bukharov [1].

The synthesis of α -decylthiophane is represented by scheme 1.



The following intermediate compounds were prepared during the synthesis of α -decylthiophane (V): α -nonylfurlylcarbinol (I), ethyl γ -ketotetradecanoate (II), 1,4-tetradecanediol (III), and 1,4-dibromotetradecane (IV), all of which have likewise not previously been described.

α -Nonylfurlylcarbinol (I) was prepared by Grignard reaction of furfural by the general method for preparation of alkylfurlylcarbinols [2].

Ethyl γ -ketotetradecanoate (II) was prepared by boiling α -nonylfurlylcarbinol in absolute alcoholic solution with addition of hydrogen chloride. Cleavage of the furan ring is here associated with a series of intermediate reversible reactions [2, 3], so that the end product may be contaminated with secondary substances.

1,4-Tetradecanediol (III) was obtained in good yield by reduction of ethyl γ -ketotetradecanoate with lithium aluminum hydride. In spite of the low degree of purity of the original ester (II), the resulting diol was extremely pure.

1,4-Dibromotetradecane (IV) was prepared by reaction of 1,4-tetradecanediol with dry HBr. This reaction is reversible, and therefore the product always contains a certain amount of diol which is difficult to remove due to the similarity in boiling points. Even treatment with concentrated H₂SO₄ failed to remove the diol.

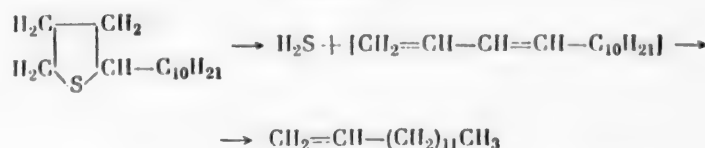
α-Decylthiophane (V) was prepared by reaction of 1,4-dibromotetradecane with an alcoholic solution of Na₂S. The reaction goes with facility and the product is obtained in good yield in pure form.

The synthesized α-decylthiophane was passed over aluminosilicate catalyst under our standard conditions [4]. Catalysis led to 57.3% of the sulfur in the original α-decylthiophane coming off as hydrogen sulfide. 1-Tetradecene and original α-decylthiophane were isolated from the liquid catalyzate.

The identity of the hydrocarbon product was confirmed by the agreement between its constants and those reported in the literature; the value found for the MR_D differed from the calculated value by only 0.05. The elemental analysis brought further confirmation.

Since the sole products of catalytic cleavage of α-decylthiophane are hydrogen sulfide and 1-tetradecene, the mechanism of cleavage of α-decylthiophane may be represented by scheme 2.

Scheme 2



Saturation of 1,3-tetradecadiene to 1-tetradecene involves intramolecular migration of hydrogen. Mercaptans are absent from the catalyzate. Cyclic sulfides accordingly do not behave like aliphatic sulfides. Under the same catalytic conditions the latter form mercaptans and alkenes [4].

EXPERIMENTAL

The synthesis of α-decylthiophane (V) involves five steps (see scheme 1).

α-Nonylfurylcarbinol (I) was prepared from 439 g of nonyl bromide in solution in 1.5 liters of absolute ether, 55 g of Mg, and 192 g of freshly distilled furfural. Yield 334 g (76%).

M. p. +3.9°, b. p. 144–145° (5 mm), n_D^{20} 1.4665, d_4^{20} 0.9326, MR_D 66.48. C₁₄H₂₄O₂. Calculated 67.03°.

Ethyl γ-ketotetradecanoate (II). Into a hot solution of 288 g of α-nonylfurylcarbinol in 320 ml of absolute alcohol was stirred an alcoholic solution of HCl (60 g of dry HCl in 400 ml of alcohol). The reaction mixture was boiled for 30 min, after which 2/3 of the alcohol was distilled off, and the residue poured into saturated K₂CO₃ solution. The supernatant oil was separated, and the aqueous layer was extracted with ether and dried with K₂CO₃. There was obtained 171.4 g (49.5%) of ethyl γ-ketotetradecanoate.

M. p. +17°, b. p. 142–144° (3 mm), n_D^{20} 1.4508, d_4^{20} 0.9227, MR_D 78.26. C₁₆H₃₀O₃. Calculated 78.14.

The elemental analysis was unsatisfactory. According to the literature the ethyl esters of γ-keto acids are not always adequately purified by numerous distillations in vacuo [1].

1,4-Tetradecanediol (III). Into an ethereal solution of lithium aluminum hydride [5], from 22.5 g of LiH and 182.5 g of AlBr₃ in 780 ml of absolute ether, was slowly stirred a solution of 120 g of ethyl γ-tetradecanoate in 190 ml of absolute ether. The reaction mixture was boiled for 3 hr. The excess of lithium aluminum hydride was cautiously decomposed with water and then with 15% sulfuric acid. The ether layer was separated and the aqueous layer extracted with ether. The extract was washed with saturated K₂CO₃ solution and dried with K₂CO₃. After distillation of the solvent, the 1,4-tetradecanediol crystallized. Yield nearly quantitative. M. p. 57.2°, b. p. 172–174° (5 mm).

Found %: C 73.17, 72.91; H 12.75, 13.00. C₁₄H₃₀O₂. Calculated %: C 72.98; H 13.12.

*The elemental analysis was not carried out since the compound easily breaks down on standing.

1,4-Dibromotetradecane (IV). A three-necked flask, fitted with stirrer, reflux condenser, and gas-leading tube, was charged with 60 g of 1,4-tetradecanediol. At 120° a stream of dry HCl was passed into the fused substance for 28 hr. The reaction product was dissolved in ether, washed with water and then with saturated K₂CO₃ solution, and dried with CaCl₂. The residue (after removal of solvent) was distilled in vacuo. Yield 82 g (88.8%).

B. p. 182–184° (9 mm), n_D^{20} 1.4957, d_4^{20} 1.2174.

α -Decylthiophane (V). The 82 g of 1,4-dibromotetradecane was boiled with a threefold excess of alcoholic solution of sodium sulfite for 3 hr, part of the alcohol was distilled off, and the residue was diluted with water for dissolution of the NaBr formed in the reaction. The supernatant oil was separated, and the aqueous layer was extracted with ether and the extract dried with CaCl₂. The compound was distilled after distillation of the solvent. Yield 44 g (83.7%).

B. p. 148.5–149° (5.5 mm), n_D^{20} 1.4804, d_4^{20} 0.8959, M_R 72.4; calc. 72.8.

Found %: C 73.80, 73.85; H 12.36, 12.34; S 13.51, 13.36. C₁₄H₂₈S. Calculated %: C 73.66; H 12.35; S 14.04.

Catalytic transformation of α -decylthiophane. Two experiments were run under the same conditions. In each case 30 g of α -decylthiophane was passed over aluminosilicate catalyst at 300°. From the two experiments was obtained 44 g of catalyzate (73.3% of the starting α -decylthiophane). The hydrogen sulfide in the exit gas was precipitated with sodium plumbite. The quantity of PbS formed during both of the experiments was 36 g, equivalent to 4.8 g of sulfur (57.3% of the content in the original α -decylthiophane). Fractionation of the catalyzate gave 4.3 g of 1-tetradecene. The compound decolorizes bromine water and alkaline KMnO₄ solution.

B. p. 80–82° (8 mm), n_D^{20} 1.4383, d_4^{20} 0.7841, M_R 66.60; calc. 66.65.

Found %: C 85.40; H 14.85. C₁₄H₂₈. Calculated %: C 85.63; H 14.38.

Literature [6]: b. p. 124.5–125° (15 mm), n_D^{20} 1.4381, d_4^{20} 0.788.

From the higher catalyzate fraction was isolated 6.1 g of α -decylthiophane with b. p. 156–158° (8 mm), n_D^{20} 1.4820, d_4^{20} 0.8927.

SUMMARY

1. α -Decylthiophane was synthesized and characterized for the first time.
2. The following intermediates, not previously described in the literature, were obtained during synthesis of α -decylthiophane: α -nonylfurylecarbinol, ethyl γ -ketotetradecanoate, 1,4-tetradecanediol, and 1,4-dibromotetradecane.
3. In presence of aluminosilicate catalyst α -decylthiophane breaks down at 300° into hydrogen sulfide and an unsaturated hydrocarbon – 1-tetradecene. Unchanged α -decylthiophane was found in the catalyzate.

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IMIDAZOLE DERIVATIVES

XXIII. 5,6-DIHYDROXY DERIVATIVES

OF BENZIMIDAZOLONE

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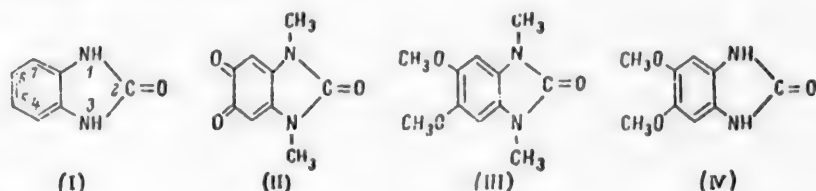
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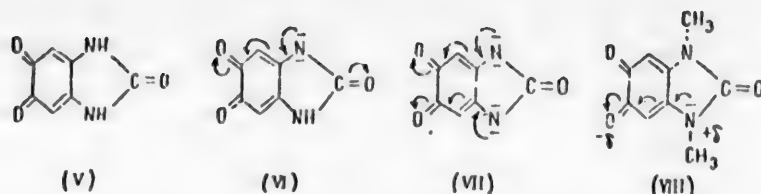
The chemical properties of quinones are known to depend on the fine structure of the starting substance which does not contain carbonyl groups [1]. In this connection a number of workers [2-4] have closely examined the influence of the structure of quinones on the magnitude of their redox potentials. A proportionality was established between the redox potential of carbocyclic o-quinones and the bond order of the carbon atoms of the starting substance at which the quinone was formed [5]. It therefore seemed of interest, in connection with a study of the fine structure of the molecule of benzimidazolone (I), to make a closer examination of the properties of the previously described [6] 5,6-dioxo-1,3-dimethylbenzimidazolone (II). This quinone was obtained not only by oxidation of the corresponding aminohydroxy and dihydroxy derivatives but also by the action of potassium nitrosodisulfonate on 5-hydroxy-1,3-dimethylbenzimidazolone.

It was found that this quinone is also very easily prepared by oxidation of 5,6-dimethoxy-1,3-dimethylbenzimidazolone (III) with nitric acid diluted with nitrous acid, ferric chloride, etc. This method is considerably simpler than the syntheses previously described. Quinone (II) is smoothly converted to the monoxime on treatment with hydroxylamine in an acid medium.



Direct transformation of o-dimethoxy derivatives into quinones has already been described (see for example [7]). 5,6-Dimethoxybenzimidazolone (IV) was found to undergo this transformation with formation of 5,6-dioxo-benzimidazolone (V). The structure of this new o-quinone was confirmed by its condensation with o-diamines to form azines and by its reduction to a colorless 5,6-dihydroxy derivative which could be purified by careful crystallization.

In contrast to compound (II), the quinone (V) contains two acidic hydrogen atoms, and therefore the color of its aqueous solutions (λ_{\max} 501 $m\mu$) is changed by alkali treatment at first to blue-violet (formation of a singly-charged anion (VI, λ_{\max} 600 $m\mu$) and then to green (formation of doubly-charged anion (VII, λ_{\max} 665 $m\mu$) with a marked fall in light absorption by (VII) (Fig. 1).



The bathochromic shift of the anion of (VII) in relation to the anion of (VI) is evidently associated with an increase in the number of free electron pairs capable of vibrating, while the hypsochromic shift is associated with a decrease in the number of localization points of the negative charge on each free electron pair

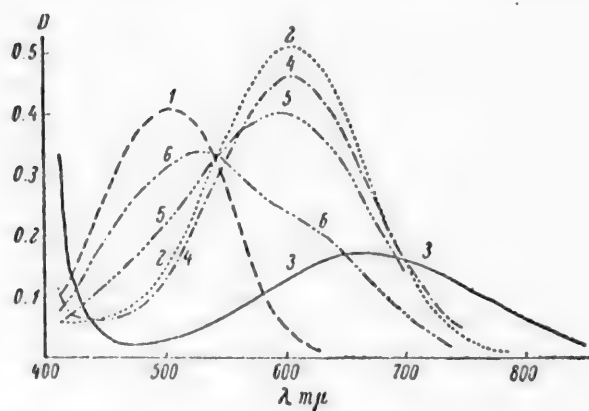


Fig. 1. Absorption spectra of solutions of 5,6-dioxo-benzimidazolone in buffer solutions ($c\ 3.25 \times 10^{-4}$ molar). PH values: 1) 2.10, 2) 9.04, 3) 12.00, 4) 10.75, 5) 7.44, 6) 6.82.

In a study of the absorption spectra of quinone (II), which is not capable of dissociation, we observed that the position of all of the maxima, and in particular of the maximum of the long-wave band of this compound, is markedly dependent on the nature of the solvent. Change-over from aqueous solutions to carbon tetrachloride solutions, for example, causes the peaks of light absorption of the quinone to be shifted to the short-wave region (Fig. 2). We see from the table below that the position of the long-wave maximum of light absorption is generally proportional to the polarity of the solvent. These changes in the absorption spectrum cannot be explained by formation of associated molecules since the position of the absorption maxima does not depend on the concentration of the solutions in the range of 10^{-3} to 10^{-5} molar. We therefore suggest that the phenomenon is the result of change in the degree of intramolecular polarization of the quinone in accordance with scheme (VIII) under the influence of the solvent molecules. A similar

effect has been found [8] with the molecule of adrenochrome whose structure is similar to that of our quinone.

Light Absorption of Quinone (II) in Different Solvents

Solvent	$\lambda_{\max} \pm 2\text{ m}\mu$
Carbon tetrachloride	453
Benzene	469
Chlorobenzene	471
Chloroform	474
Acetone	475
Nitrobenzene	479
Methanol	485
Water	516

With leuco compounds the quinones (II) and (V) very smoothly form quinhydrones which are fairly stable and can be recrystallized from solvents. Using these compounds in the form of a 50% mixture of quinone and quinhydrone, we were easily able to determine the redox potentials of the quinones under investigation.

The value found for 5,6-dioxo-1,3-dimethylbenzimidazolone (II) was 587 mv (18°), and that for 5,6-dioxobenzimidazolone was 585 mv (18°). The corrected values are respectively 487 mv and 485 mv [5]. Quinones (II) and (V) have very similar redox potentials. These data, in association with the similarity in the electronic absorption spectra of the quinones (Fig. 2), are evidence of the formal structural similarity of the

compounds and of the similarity of the fine structure of analogs of benzimidazolone and 1,3-dialkylbenzimidazolone which we had previously reported [9].

Knowing the redox potentials of quinones (II) and (V), we can make use of the Badger relation [5] between redox potential of o-quinones and the bond order of the quinone-forming carbon atoms. This relation was established for carbocyclic compounds but does not appear to have been applied to heterocyclics.

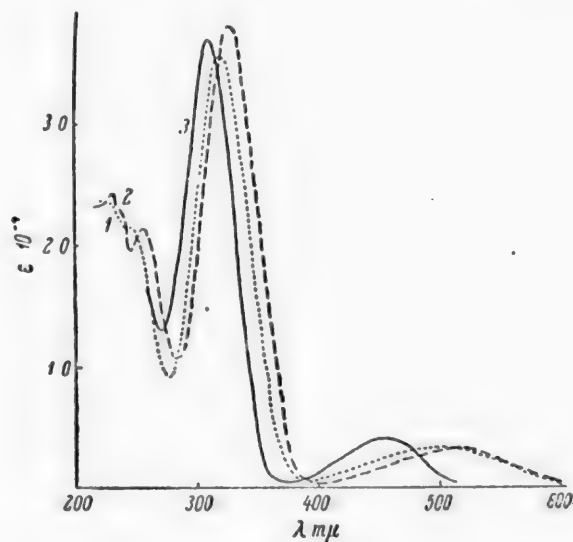


Fig. 2. Absorption spectra of solutions: 1) 5,6-dioxo-benzimidazolone in 0.01% aqueous acetic acid (c 1.88×10^{-4} and 0.378×10^{-4} molar, λ_{\max} 228, 246, 321 and 502 $m\mu$; λ_{\min} 243, 278, 243 $m\mu$); 2) 5,6-dioxo-1,3-dimethylbenzimidazolone in water (c 1.94×10^{-4} and 0.394×10^{-4} molar, λ_{\max} 232, 257, 330 and 516 $m\mu$; λ_{\min} 226, 247, 284 and 398 $m\mu$); 3) 5,6-dioxo-1,3-dimethylbenzimidazolone in carbon tetrachloride (c 1.41×10^{-4} and 0.282×10^{-4} molar, λ_{\max} 312 and 243 $m\mu$; λ_{\min} 270 and 371 $m\mu$).

On the basis of this relation we can find that the bond order between carbon atoms 5 and 6 of benzimidazolone is 1.73. This is very close to the value (1.738) of the 1-2 bond order in the naphthalene molecule (for benzene the C-C bond order is 1.667). The electron cloud of the benzene ring of benzimidazolone is consequently deformed and the degree of double-bonding between its carbon atoms 5 and 6 is actually greatly increased.

In previous communications we compared the reactivities of 5-hydroxy- and 5-amino derivatives of benzimidazolone and of 2-hydroxy- and 2-amino-substituted naphthalenes [6, 10]. We showed that their behavior is absolutely analogous in cationoid substitution reactions. We therefore inferred that the degree of double-bonding between carbon atoms 5 and 6 of benzimidazolone is increased just as is the case between carbon atoms 1 and 2 of naphthalene. This reasoning was confirmed by determinations of the redox potentials of quinones (II) and (IV) and in turn of the bond order between carbon atoms 5 and 6. We are therefore justified in claiming to have been the first to observe in the case of benzimidazolone the type of deformation of the electron cloud of the benzene ring that Mills and Nixon had erroneously attributed to the benzene ring of the hydrindene molecule [11].

EXPERIMENTAL

5,6-Dioxobenzimidazolone. Sodium nitrite and 5,6-dimethoxybenzimidazolone (equal parts by weight) were dissolved in the tenfold quantity of 50% alcohol, and concentrated hydrochloric acid was added dropwise in the cold to the solution until it was acidic to Congo. The precipitate was filtered and twice crystallized from a large volume of water containing a few drops of acetic acid. The product formed dark-red, lustrous, small, fine needles (yield 40-45%). It did not melt at 300°. Insoluble in chloroform and acetone, very sparingly soluble in methyl and ethyl alcohols, chlorobenzene, benzene, dioxane, nitrobenzene, quinoline, and acetic acid. Crystallization from water is accompanied by considerable losses of the substance.

The quinone is soluble in caustic alkali and sodium carbonate and comes out of solution on acidification. Heating of the alkaline solution changes the color to dark-brown, and the quinone cannot then be isolated on acidification. The solution in concentrated sulfuric acid has a violet color.

Found %: C 51.25, 51.18; H 2.57, 2.50; N 17.13, 17.03. $C_7H_4O_3N_2$. Calculated %: C 51.20; H 2.44; N 17.08.

5,6-Dioxo-1,3-dimethylbenzimidazolone, which we have fully described previously, can be prepared on the same lines as 5,6-dioxobenzimidazolone by oxidation of the corresponding dimethoxy derivative. In the present case the quinone must in addition be extracted from the solution by chloroform because it is highly soluble in aqueous alcohol.

5,6-Dihydroxybenzimidazolone. To a boiling solution of 0.5 g of ascorbic acid in 20 ml of water was added 0.15 g of 5,6-dioxobenzimidazolone in small portions; after the solution had cooled, the precipitate was filtered and recrystallized from water. The resulting slightly grayish, colorless, fine needles (weight 50 mg) did not melt at 300°. Sparingly soluble in cold water, alcohol, and acetic acid; insoluble in benzene, chloroform, and carbon tetrachloride, and soluble in pyridine.

Found %: N 16.90, 16.78. $C_7H_6O_3N_2$. Calculated %: N 16.86.

Quinhydrone from 5,6-dioxobenzimidazolone. A solution of 300 mg of the quinone in 300 ml of water was prepared. Into one-half of the hot solution was carefully stirred dropwise a 3% aqueous solution of ascorbic acid until color disappeared. The two portions of solution were then mixed and quickly cooled. The resulting crystalline precipitate was filtered and washed with water (4 x 15 ml). There was obtained 230 mg of substance in the form of small, violet-black needles, soluble in water and organic solvents, not melting at 300°.

Found %: C 51.12, 51.24. H 3.21, 3.23. $C_{14}H_{10}O_6N_4$. Calculated %: C 50.91; H 3.05.

Quinhydrone from 5,6-dioxo-1,3-dimethylbenzimidazolone. A concentrated alcoholic solution of ascorbic acid was carefully added dropwise to a solution of 500 mg of quinone in 50 ml of hot alcohol until the solution was decolorized. Addition of 500 mg of quinone was then made and the solution cooled. The crystals were filtered and recrystallized from alcohol. Long, dark-violet needles (weight 800 mg) with m. p. 250–254° (decomp.). Insoluble in benzene and carbon tetrachloride, sparingly soluble in ethyl acetate, easily soluble in pyridine; crystallizes from dioxane, alcohol, and ethyl acetate; very much less soluble in alcohol than the original quinones.

Found %: C 55.95, 55.90; H 4.27, 4.96. $C_{18}H_{18}O_6N_4$. Calculated %: C 55.95; H 4.70.

Phenazine from o-phenylenediamine and 5,6-dioxobenzimidazolone. To a suspension of 200 mg of quinone in 25 ml of boiling glacial acetic acid was added 400 mg of o-phenylenediamine in small portions. The mixture was heated at the boil for a few minutes until the whole of the quinone had dissolved. Boiling water (25 ml) was then added, and the solution was treated with carbon and cooled. The azine was crystallized three times from 60% acetic acid. The compound does not melt at 300°. It is insoluble in chloroform, carbon tetrachloride, and benzene, soluble in dioxane and acetic acid, sparingly soluble in alcohol. The solution in alkali and in concentrated sulfuric acid has a red color.

Found %: N 23.86, 23.75. $C_{13}H_8ON_4$. Calculated %: N 23.72.

Phenazine from o-phenylenediamine and 5,6-dioxo-1,3-dimethylbenzimidazolone. A mixture of 400 mg of o-phenylenediamine, 400 mg of quinone, and 7 ml of acetic acid was brought to the boil and boiled for several minutes. After cooling, the precipitate was filtered, washed with alcohol on the filter, and recrystallized from alcohol and then from acetic acid. There was obtained 300 mg of product in the form of bright-yellow, small, fine needles which did not melt at 300° and exhibited a vivid green fluorescence on exposure to ultra-violet light. Readily soluble in benzene, acetic acid, dioxane, and chloroform; crystallizes from alcohol. The solution in concentrated sulfuric acid has a red color.

Found %: N 21.13, 21.36. $C_{15}H_{12}ON_4$. Calculated %: N 21.21.

Oxime from 5,6-dioxo-1,3-dimethylbenzimidazolone. To a solution of 0.337 g of quinone in 70 ml of hot water was added 1.5 g of hydroxylamine hydrochloride. The solution was heated to boiling, transferred to a graduated flask, cooled, and made up to 100 ml. The resulting precipitate was filtered and twice crystallized from water. The fine, orange needles (weight 0.250 g) melted unsharply at 214° (decomp.) after drying at 105° for half an hour. The compound crystallizes from water, alcohol, dioxane, and ethyl acetate; soluble in acetic acid, difficultly soluble in chloroform, insoluble in benzene and ligroine. Addition of Coprantin Salt [12] to a solution of the oxime and sodium acetate in water leads to immediate precipitation of the brown copper complex of the oxime which dissolves when hydrochloric acid is added.

The mother liquor from the oxime synthesis was diluted five times and potentiometrically titrated with 0.1 N NaOH; reaction of the quinone with hydroxylamine hydrochloride was found to release exactly one equivalent of acid.

Found %: N 20.11, 20.16. $C_9H_9O_3N_3$. Calculated %: N 20.28.

Measurement of redox potentials. The instrument was a LP-5 potentiometer, and a platinum-saturated calomel electrode cell was used*. The quinhydrone (20-40 mg) was placed in an acetate-phosphate-borate buffer [pH of 2 to 4 for quinone (II) and of 1-2 for quinone (V)]. The solution was stirred and the potential measured without delay (three measurements in each buffer). The quinhydrone was then crystallized and the measurements repeated. In this second series the results agreed with those in the first. The measuring error was estimated at 1%.

SUMMARY

1. Direct oxidation of 5,6-dimethoxy derivatives of benzimidazolone gave its 5,6-dioxo derivatives which readily form quinhydrones with leuco compounds.

2. Results of measurement of the redox potentials of the prepared o-quinones reflect the considerably increased bond order of carbon atoms 5 and 6 in the benzimidazolone molecule.

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* A correction for the potential of the saturated calomel electrode in relation to the hydrogen electrode was introduced in calculations by [1].

** Original Russian pagination. See C. B. translation.

PYRAZOLES

XII. HYDROXYMETHYLATION AND CHLOROMETHYLATION

OF 1-SUBSTITUTED PYRAZOLES

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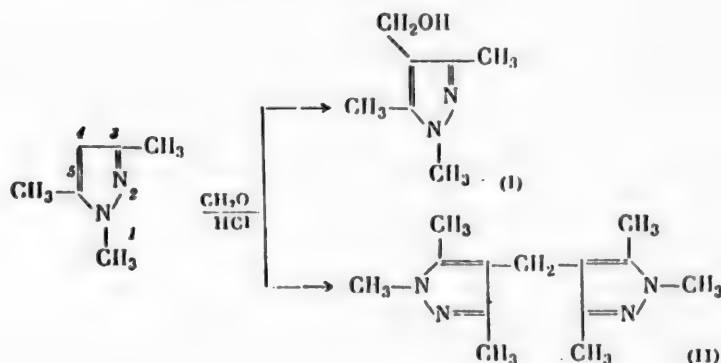
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In a study of the hydroxymethylation of pyrazoles with a free NH group, it was found [1] that in neutral and alkaline media they all smoothly give 1-hydroxymethyl derivatives. In acidic media they gave polymers, which were not examined closely, and a small quantity of 1,4-dihydroxymethyl-3,5-dimethylpyrazole. It has been reported [2] that in a hydrochloric acid medium 1,3,5-trimethylpyrazole with paraformaldehyde (20°, 15 days) gives the 4-hydroxymethyl derivative (yield not mentioned). 1-Phenylpyrazole has been hydroxymethylated with a yield of 57%; under more drastic conditions the formation of dipyrazolymethane was also observed but in a yield of only 10% [3].

Our first attempts at hydroxymethylation of 1,3,5-trimethylpyrazole under classical conditions (anhydrous zinc chloride, dry hydrogen chloride) were unsuccessful. Some pyrazoles gave remarkably stable complexes with zinc chloride (we also observed formation of this type of complex previously [4]); moreover the zinc hydroxide complicated the further treatment. In the absence of zinc chloride and in presence of concentrated hydrochloric acid (2-4 hr at 50-70°) we effected hydroxymethylation of some pyrazoles in position 4 of the ring (I), but at the same time dipyrazolymethanes were formed (II).



The structure of the prepared compounds was confirmed by oxidation of two of them (1,3,5-trimethyl-4-hydroxymethylpyrazole and 1-phenyl-3,5-dimethyl-4-hydroxymethylpyrazole) with potassium permanganate to the corresponding 4-carboxylic acids. The constants of the latter were the same as those reported in the literature. It is interesting to note that the hydroxymethyl group in position 4 of the ring of 1-alkylpyrazoles is extremely labile: under the action of acidic agents (thionyl chloride, hydrogen chloride) or simply by the action of hot concentrated hydrochloric acid 1,3,5-trimethyl-4-hydroxymethylpyrazole (I) is easily converted to di-

(1,3,5-trimethyl-4-pyrazolyl)-methane (II). This is evidently due to the phenomenon of "vinylogy", i. e. the hydroxymethyl group in position 4 behaves like the hydroxymethyl group in position 1 which is easily removed by treatment with acidic agents [1].

For this reason we were unable to obtain 4-chloromethyl derivatives by treating hydroxymethyl derivatives of 1-alkylpyrazoles with thionyl chloride. However, whenever the pyrazole ring contained phenyl groups in position 1 (with exception of 1-phenyl-3,5-dimethylpyrazole) we always obtained not hydroxymethyl but chloromethyl derivatives. In the case of 1-phenyl-3-methyl-5-chloropyrazole and 1,3,5-triphenylpyrazole only chloromethyl derivatives were obtained without traces of dipyrazolymethanes.

EXPERIMENTAL

1,3,5-Trimethyl-4-hydroxymethylpyrazole (I). Into a three-necked flask, fitted with reflux condenser, thermometer, and bubbler, were introduced 11 g of 1,3,5-trimethylpyrazole [4] and 30 ml of concentrated hydrochloric acid. A stream of dry hydrogen chloride was passed through for 15 min and the mixture was heated to 50°. To the reaction mixture was then added 3.5 g of paraformaldehyde and the temperature raised to 60°. At 60–65° a stream of hydrogen chloride was admitted until the paraformaldehyde had completely dissolved (~ 4 hr). After cooling, the reaction mass was made alkaline, with cooling, by 40% sodium hydroxide solution and extracted with butanol. Fractionation of the butanol extract gave 8 g (57%) of 1,3,5-trimethyl-4-hydroxymethylpyrazole with b. p. 143–145° (10 mm), m. p. 82–83° (from benzene) [2].

Found %: C 58.98, 58.85; H 9.09, 9.01. $C_7H_{12}ON_2$. Calculated %: C 59.33; H 8.63.

Picrate: m. p. 90–91° (from alcohol).

Found %: N 19.01, 18.97. $C_7H_{12}ON_2 \cdot C_6H_3O_7N_3$. Calculated %: N 18.90.

Di-(1,3,5-trimethyl-4-pyrazolyl)-methane (II). a) A stream of dry hydrogen chloride was passed for 2 hr into a mixture of 11 g of 1,3,5-trimethylpyrazole, 3.5 g of paraformaldehyde, and 25 ml of dichloroethane at 50–55°, and the reaction mass was boiled for 2.5 hr; 25 ml of dilute hydrochloric acid was then added, the mixture was cooled, and the aqueous layer collected. The latter was neutralized with potassium carbonate, extracted with chloroform, and fractionally distilled to give 9.8 g (84.4%) of di-(1,3,5-trimethyl-4-pyrazolyl)-methane with b. p. 197–202° (3 mm), m. p. 66–67° (from ligroine).

Found %: C 67.12, 66.95; H 8.83, 8.78; N 24.28, 24.07. $C_{13}H_{20}N_4$. Calculated %: C 67.20; H 8.67; N 24.15.

Dipicrate; m. p. 191–192° (from alcohol).

Found %: C 43.32, 43.25; H 3.96, 3.90; N 20.43, 20.28. $C_{13}H_{20}N_4 \cdot 2C_6H_3O_7N_3$. Calculated %: C 43.33; H 3.73; N 20.28.

b) It was also prepared by heating 11 g of 1,3,5-trimethylpyrazole, 8 g of dimethylamine hydrochloride, and 3 g of paraformaldehyde in an ampoule to 190° for 4 hr. After cooling, the reaction mass was dissolved in 50 ml of water and made alkaline with 40% sodium hydroxide solution. The resulting oil was separated and fractionated in vacuo. Yield 8.3 g (71.5%), b. p. 195–197° (2 mm), m. p. 67°.

Dipicrate: m. p. 192–193° (from alcohol).

c) It was also prepared in 75% yield by boiling 1 mole of paraformaldehyde with 1 mole of 1,3,5-trimethylpyrazole for 5 hr in 250 ml of concentrated hydrochloric acid or 200 ml of 50% sulfuric acid. Increase in the proportion of paraformaldehyde to 3 moles per mole of pyrazole or its decrease to $\frac{1}{2}$ mole per mole, or lowering of the heating period to 2 hr, hardly affected the yield of compound (II). In all these cases no hydroxymethyl derivative (I) was obtained.

Attempts to synthesize 1,3,5-trimethyl-4-chloromethylpyrazole. In a three necked flask, fitted with stirrer, dropping funnel, and reflux condenser were placed 7 g of 1,3,5-trimethyl-4-hydroxymethylpyrazole and 25 ml of anhydrous carbon tetrachloride. Thionyl chloride (7 ml) was slowly added dropwise with cooling. After this operation the reaction mass was stirred for 2 hr at room temperature and then cautiously poured into 25 ml of cold water with thorough stirring. The aqueous layer was separated, neutralized with sodium bicarbonate, and extracted with butanol. The butanol extracts were fractionated to give 3.5 g (60%) of di-(1,3,5-trimethyl-4-

pyrazolyl)-methane with b. p. 206–209° (5 mm), m. p. 66° (from water).

Dipicrate: m. p. 192–193° (from alcohol). No depression in admixture with the dipicrate described above.

Into a mixture of 50 ml of anhydrous benzene and 7 g of 1,3,5-trimethyl-4-hydroxymethylpyrazole, heated to boiling, was passed a strong stream of dry hydrogen chloride for an hour. At the same time the benzene was distilled off. The mass was worked up in the usual way to give 3.7 g (64%) of compound (II) with b. p. 211–216° (9 mm).

Dipicrate: m. p. 192° (from alcohol). No depression of melting point in admixture with the dipicrate described above.

1-Ethyl-4-hydroxymethyl-3,5-dimethylpyrazole was prepared similarly to 1,3,5-trimethyl-4-hydroxymethylpyrazole from 6.2 g of 1-ethyl-3,5-dimethylpyrazole [4], 2 g of paraformaldehyde, and 25 ml of concentrated hydrochloric acid. Yield 5.2 g (65%), b. p. 145–147° (10 mm), m. p. 72–73° (from ligroine).

Found %: N 18.41, 18.41. $C_8H_{14}ON_2$. Calculated %: N 18.15.

Di-(1-ethyl-3,5-dimethyl-4-pyrazolyl)-methane was prepared by heating of 6.2 g of 1-ethyl-3,5-dimethylpyrazole, 2 g of paraformaldehyde, and 10 ml of concentrated hydrochloric acid in a sealed tube at 140° for 4 hr. The mass was worked up in the usual way to give 6 g (83.4%) of compound with b. p. 196–197° (14 mm), m. p. 40–41° (from ligroine).

Found %: N 21.69, 21.40. $C_{15}H_{24}N_4$. Calculated %: N 21.51.

Dipicrate: m. p. 202–203° (from alcohol).

Found %: N 20.04, 19.90. $C_{15}H_{24}N_4 \cdot 2C_6H_5O_7N_3$. Calculated %: N 19.51.

Hydroxymethylation of 1-phenyl-3,5-dimethylpyrazole. A mixture of 17.2 g of 1-phenyl-3,5-dimethylpyrazole [4], 3.6 g of paraformaldehyde, and 25 ml of concentrated hydrochloric acid was heated to the boil while a stream of hydrogen chloride was passed through for 4 hr. The reaction mass was then cooled, neutralized with ammonia, and extracted with butanol. Fractional distillation gave 3.1 g (15.4%) of 1-phenyl-4-hydroxymethyl-3,5-dimethylpyrazole in the form of a viscous, glassy liquid with b. p. 155–160° (2 mm).

Found %: N 13.75, 13.60. $C_{12}H_{14}ON_2$. Calculated %: N 13.85.

There was also isolated 5.9 g (33.1%) of di-(1-phenyl-3,5-dimethyl-4-pyrazolyl)-methane with b. p. 255–263° (3 mm), m. p. 116–117° (from ligroine).

Dipicrate: m. p. 144–145° (from alcohol).

Found %: C 51.76, 51.95; H 4.00, 3.84; N 17.03, 17.02. $C_{23}H_{24}N_4 \cdot 2C_6H_5O_7N_3$. Calculated %: C 51.60; H 3.71; N 17.14.

Chloromethylation of 1-phenyl-3-methyl-5-chloropyrazole. Reaction of 9.6 g of 1-phenyl-3-methyl-5-chloropyrazole [5] with 2 g of paraformaldehyde was effected by heating in presence of 20 ml of concentrated hydrochloric acid for 2 hr. The mass was worked up in the usual manner to give 8.5 g (70.0%) of 1-phenyl-3-methyl-5-chloro-4-chloromethylpyrazole with b. p. 164–165° (8 mm), m. p. 39° (from ligroine).

Found %: C 55.10, 54.93; H 5.06, 4.88; N 11.69, 11.50. $C_{11}H_{10}N_2Cl_2$. Calculated %: C 54.80; H 4.95; N 11.50.

Chloromethylation of 1-phenyl-3-methylpyrazole. A mixture of 15.8 g of 1-phenyl-3-methylpyrazole, 3 g of paraformaldehyde, and 25 ml of concentrated hydrochloric acid was heated for 1.5 hr. The mass was worked up in the usual manner to give 3.2 g (15.5%) of 1-phenyl-3-methyl-4-chloromethylpyrazole with b. p. 170–174° (4 mm), m. p. 73–74° (from ligroine).

Found %: C 64.20, 64.17; H 5.64, 5.44. $C_{11}H_{11}N_2Cl$. Calculated %: C 63.90; H 5.37.

There was also obtained 4.9 g (30%) of di-(1-phenyl-3-methyl-4-pyrazolyl)-methane with b. p. 265–268° (3 mm), m. p. 83–84° (from ligroine).

Found %: C 76.74, 76.50; H 6.28, 6.27. $C_{21}H_{20}N_4$. Calculated %: C 76.78; H 6.14.

Chloromethylation of 1,3,5-triphenylpyrazole. A mixture of 5 g of 1,3,5-triphenylpyrazole, 0.4 g of paraformaldehyde, and 5 ml of concentrated hydrochloric acid was heated in an ampoule at 170° for 4 hr. The mixture was then made alkaline with 40% sodium hydroxide solution, and the crystals were collected, washed with water, and recrystallized from benzene. Yield 4.8 g (82.7%) of 1,3,5-triphenyl-4-chloromethylpyrazole with m. p. 118–119° (from benzene).

Found %: N 7.92, 7.90. $C_{22}H_{17}N_2Cl$. Calculated %: N 8.12.

1,3,5-Trimethylpyrazole-4-carboxylic acid. To a hot solution of 1 g of 1,3,5-trimethyl-4-hydroxymethylpyrazole in 20 ml of water was added 0.8 g of potassium permanganate portionwise with shaking. Heating was continued for an hour. After the mass had cooled, the manganese dioxide was filtered off and twice washed with 10–15 ml portions of hot water. The filtrates were combined and evaporated to a volume of 5 ml. The 1,3,5-trimethylpyrazole-4-carboxylic acid was precipitated by 1 : 1 hydrochloric acid. The crystals (0.6 g) were collected and washed with water. M. p. 216–217° (from a mixture of benzene and ligroine), in agreement with the literature [6].

Found %: N 18.42, 18.38. $C_7H_{10}O_2N_2$. Calculated %: N 18.15.

1-Phenyl-3,5-dimethylpyrazole-4-carboxylic acid. Into 1 g of 1-phenyl-3,5-dimethyl-4-hydroxymethylpyrazole in 25 ml of water in a 100 ml beaker was stirred portionwise 1.05 g of potassium permanganate; stirring and heating were continued for 15 min. The precipitated manganese dioxide was filtered and twice washed on the filter with hot water. The filtrates were combined and evaporated. The solution was then cooled and doubly diluted hydrochloric acid added. The precipitated 1-phenyl-3,5-dimethylpyrazole-4-carboxylic acid (0.7 g) had m. p. 196–197° (from benzene) in agreement with the literature [7].

SUMMARY

1. It was shown that treatment of 1-alkylpyrazoles with paraformaldehyde and hydrochloric acid leads to hydroxymethylation in position 4 of the ring. Dipyrazolymethanes are formed concurrently.
2. In the case of 1-phenylpyrazoles the sole reaction in general is chloromethylation in position 4 of the ring.

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INVESTIGATIONS OF β - AND γ -PYRIDYLTHIAZOLINES. I.

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It has been shown [1] that 2-substituted Δ^2 -thiazolines are of interest in the search for substances possessing pharmacological and antibacterial activity. We thought it might be useful in this connection to prepare derivatives of thiazoline with a γ -pyridine residue in position 2 since these compounds can be regarded as cyclic substituted thioamides of isonicotinic acid, and some members of the latter class exhibit a relatively high anti-tubercular activity [2].

We prepared 2- γ -pyridyl- Δ^2 -thiazoline and 2- γ -pyridyl-5-methyl- Δ^2 -thiazoline by condensation of mercaptoethylamine and β -mercaptopropylamine with 4-pyridinenitrile.

The most convenient route to 2-(γ - and β -pyridyl)- Δ^2 -thiazoline-4-carboxylic acid was found to be reaction of iminoesters with the methyl ester of cysteine (i.e. of β -mercaptoalanine) [3]. Iminoesters of γ - and β -pyridine-carboxylic acids have not been described in the literature. We prepared them by treating a solution of equimolar quantities of pyridinenitrile and anhydrous alcohol in chloroform with dry hydrogen chloride and effecting condensation with the methyl ester of cysteine in aqueous solution at pH 6. The resulting methyl ester of 2-(γ -pyridyl)- Δ^2 -thiazoline-4-carboxylic acid was converted to the free acid and its derivatives - amide, hydrazide, and hydroxamic acid. Analogs were prepared by starting from nicotinonitrile.

A study of the activity of these compounds toward tubercular mycobacteria showed that they inhibit the growth of such organisms at relatively high concentrations (1:4500 to 1:16000), whereas isonicotinic acid thioamide is very much more active (bacteriostatic action manifested at 1:512000 dilution*).

EXPERIMENTAL

2-(γ -Pyridyl)- Δ^2 -thiazoline (I). A solution of 2 g of mercaptoethylamine and 2.5 g of 4-pyridinenitrile in 20 ml of anhydrous alcohol was boiled and stirred in a nitrogen atmosphere until ammonia ceased to be evolved (6 hr). The alcohol was then taken off in vacuo and ether was added to the residue. Addition of ether and its removal in vacuo were repeated a number of times. The product crystallized and was recrystallized from a 1:1 mixture of heptane and benzene. Yield quantitative. Colorless prisms, m. p. 72-73°, soluble in alcohols, ether, benzene, and the majority of other organic solvents; insoluble in water.

Found %: C 58.58; H 5.00; N 17.13; S 19.20. $C_8H_8N_2S$. Calculated %: C 58.51; H 4.91; N 17.06; S 19.53.

Picrate: m. p. 179-180° (from alcohol).

Found %: C 42.89; H 2.91; N 17.58; S 7.97. $C_{14}H_{11}O_7N_3S$. Calculated %: C 42.76; H 2.82; N 17.81; S 8.15.

5-Methyl-2-(γ -pyridyl)- Δ^2 -thiazoline (II). A mixture of 3.42 g of β -mercaptopropylamine hydrochloride, 20 ml of sodium ethoxide solution (0.62 g Na), and 2.5 of 4-pyridinenitrile was boiled in a nitrogen atmosphere

*The tuberculostatic activities were examined in the department of chemotherapy of the All-Union Scientific Research Institute for Chemical Pharmaceutics (VNIKhFI) under the direction of G. N. Pershin.

until nitrogen ceased to come off (5 hr). The precipitated sodium chloride was filtered off, the solvent removed in vacuo, and the oily residue dissolved in anhydrous ether. The solution was filtered from inorganic salts and the ether was distilled off to leave a yellow oil soluble in organic solvents. It gave a picrate in about 30% yield; m.p. 146-147° (from ethyl alcohol).

Found %: C 44.06; H 3.18; N 16.95; S 7.96. $C_{15}H_{13}O_7N_5S$. Calculated %: C 44.23; H 3.22; N 17.19; S 7.87.

Iminoethyl ester of isonicotinic acid (III). Dry hydrogen chloride was passed into a solution of 9 g of 4-pyridinenitrile in 75 ml of anhydrous chloroform and 5.2 ml of anhydrous alcohol cooled to 0°. The temperature of the reaction mixture was not allowed to rise above 5°. When the crystals formed on the liquid surface had been converted into a transparent, oily layer the stream of hydrogen chloride was stopped and the reaction mixture was left overnight in a refrigerator. The top layer crystallized. The reaction mass was then added to cooled 50% potassium hydroxide solution (until the mass was alkaline to litmus), and the base was extracted with chloroform. The extract was washed with water and dried with potassium carbonate. Removal of the solvent in vacuo at room temperature left 12.35 g of substance (~85%) in the form of a faint-yellow oil which was stable only when kept in a refrigerator. It forms a picrate and hydrochloride which break down in course of purification.

Picrate: m.p. 114-115°.

Hydrochloride: m.p. 245-247°.

Methyl ester of 2-(γ -pyridyl)- Δ^2 -thiazolinecarboxylic acid (IV). Cysteine methyl ester hydrochloride, prepared from 6.04 g of cysteine [3], was dissolved in 12 ml of nitrogen-saturated water, and the solution was neutralized by concentrated ammonia solution to pH 3 in presence of a stream of nitrogen. To the resulting solution was added 12.35 g of ester (III) dissolved in 30 ml of ether. The mixture (pH ~ 6) was shaken for 30 hr. The ethereal layer was separated and the aqueous layer extracted with ether. The combined ethereal solutions were dried with magnesium sulfate in presence of carbon. The compound crystallized (after the ether had been taken off in vacuo) and was washed with water. Yield 7 g (64% calculated on the cysteine). Recrystallization from 1:1 benzene-heptane gave a product with m.p. 71-72°. Colorless prisms, insoluble in ligroine, sparingly soluble in boiling water, easily soluble in alcohols, ether, and other organic solvents.

Found %: C 54.06; H 4.50; N 12.49; S 14.39. $C_{10}H_{10}O_2N_2S$. Calculated %: C 54.04; H 4.54; N 12.60; S 14.43.

2-(γ -Pyridyl)- Δ^2 -thiazoline-4-carboxylic acid (V). Into 1.11 g of ester (IV) were stirred 12.76 ml of 0.396 N barium hydroxide solution and a drop of phenolphthalein solution. The alkalinity decreased after 20-40 min, and a further 2 ml of the barium hydroxide solution was therefore added. Stirring was continued for 5 hr at room temperature. The precipitated barium salt was filtered off and treated with 1 N sulfuric acid. The 2-(γ -pyridyl)- Δ^2 -thiazoline-4-carboxylic acid came down in admixture with barium sulfate. The mixed precipitate was extracted three times with hot alcohol and the extract decanted from the solid residue. Recrystallization from alcohol gave 0.55 g (54.4%) of substance with m.p. 174-175°. Fine, colorless prisms, soluble in boiling water, alcohol, ethyl acetate, insoluble in ether and chloroform.

Found %: C 52.09; H 3.79; N 13.52; S 15.11. $C_9H_9O_2N_2S$. Calculated %: C 51.91; H 3.87; N 13.45; S 15.39.

2-(γ -Pyridyl)- Δ^2 -thiazoline-4-carboxylic acid amide (VI). To a solution of 3.33 g of ester (IV) in 20 ml of methanol was added 25 ml of concentrated ammonia; colorless crystals at once started to come out. The reaction mixture was shaken for 3 hr, and the crystals were filtered and washed with aqueous alcohol. Yield 2.3 g (90%) of amide. M.p. 178-179° (decomp.) (from alcohol). Colorless plates, soluble in hot alcohol and water, insoluble in benzene and ether.

Found %: C 52.09; H 4.60; N 20.44; S 15.53. $C_9H_9ON_3S$. Calculated %: C 52.17; H 4.38; N 20.28; S 15.47.

2-(γ -Pyridyl)- Δ^2 -thiazoline-4-hydroxamic acid (VII). Hydroxylamine hydrochloride (0.14 g) in anhydrous methyl alcohol (10 ml) was neutralized with sodium methoxide. Absolute ether was added to the solution, the sodium chloride filtered off, the ether distilled in vacuo, 1.11 g of ester (IV) added to the residual methanolic solution, and the mixture stirred at room temperature. Crystals appeared in the solution after 0.5 hr, and after 3 hr these were filtered off and washed with alcohol. Yield 0.82 g (73.9%). M.p. 165-166° (decomp.) (from 50% alcohol). Fine, colorless prisms, soluble in water, less readily soluble in alcohol and dioxane, insoluble in acetone, ethyl acetate, chloroform, and ether.

Found %: C 48.35; H 4.10; N 18.73; S 14.46. $C_8H_9O_2N_3S$. Calculated %: C 48.42; H 4.07; N 18.82; S 14.36.

2-(γ -Pyridyl)- Δ^2 -thiazoline-4-carboxylic acid hydrazide (VIII). Ester (IV) (1.11 g) in methyl alcohol (20 ml) and hydrazine hydrate (0.34 g) were stirred at room temperature for 5 hr. During this operation a precipitate gradually came down. The hydrazide (yield quantitative) melted at 166-167° (decomp.) after recrystallization from 80% alcohol. Colorless prisms, sparingly soluble in water, alcohol, and dioxane, insoluble in benzene, ether and chloroform.

Found %: C 48.64; H 4.52; N 24.99; S 14.50. $C_9H_{10}ON_4S$. Calculated %: C 48.63; H 4.53; N 25.21; S 14.42.

Iminoethyl ester of nicotinic acid (IX). Prepared from 12 g of β -pyridinenitrile by the method described for the γ -analog. A yellow oil, soluble in organic solvents, insoluble in water. Yield 14.9 g (86%).

Picrate: m.p. 108-110°.

Hydrochloride: m.p. 224-226°.

Methyl ester of 2-(β -pyridyl)- Δ^2 -thiazoline-4-carboxylic acid (X). A mixture of cysteine methyl ester (from 8 g of cysteine) and iminoester (IX), prepared under the conditions for preparation of ester (IV), was stirred mechanically for 24 hr, and worked up in similar fashion. Removal of the solvent left a yellowish oil that distilled in vacuo at 178-179° (0.4-0.6 mm). Yield 10.4 g (70.9%). A yellow oil, insoluble in water and ligroine, soluble in alcohols and other organic solvents.

Picrate: m.p. 131-132° (from alcohol).

Found %: C 42.12; H 2.89; N 15.47; S 7.46. $C_{16}H_{13}O_3N_5S$. Calculated %: C 42.50; H 2.91; N 15.52; S 7.12.

Hydrochloride: m.p. 126.5-129° (from a mixture of alcohol and hydrogen chloride-containing ether).

Found %: Cl 23.89. $C_{10}H_{12}O_2N_2SCl_2$. Calculated %: Cl 24.04.

2-(β -Pyridyl)- Δ^2 -thiazoline-4-carboxylic acid (XI). A mixture of 1.66 g of ester (X) and 20 ml of 0.394 N barium hydroxide solution was stirred for 3 hr on a water bath. After cooling, 8.8 ml of 1 N sulfuric acid was added. The precipitated mixture of barium sulfate and acid (XI) was filtered and extracted three times with hot alcohol (100 ml each time). The alcoholic solution was decanted and treated with carbon, and the solvent was partly taken off in vacuo. Yield 1.25 g (80.4%) of crystalline acid (XI). M.p. 179-180 (decomp.) (from alcohol). Fine, colorless crystals, soluble in boiling water, alcohol, and ethyl acetate, insoluble in chloroform, benzene, and ether.

Found %: C 51.59; H 3.38; N 13.13; S 15.17. $C_8H_8O_2N_2S$. Calculated %: C 51.91; H 3.87; N 13.45; S 15.39.

2-(β -Pyridyl)- Δ^2 -thiazoline-4-carboxylic acid amide (XII). A solution of 1.11 g of ester (X) in 1 ml of methyl alcohol and 10 ml of concentrated ammonia were shaken for 3 hr. The resulting crystals were filtered and washed with aqueous alcohol. Yield 0.95 g (92.2%). M.p. 178-179° (decomp.) (from alcohol). Colorless plates, sparingly soluble in alcohol and water, insoluble in chloroform and ether.

Found %: C 52.38; H 4.42; N 20.28; S 15.42. $C_8H_9ON_3S$. Calculated %: C 52.17; H 4.38; N 20.28; S 15.47.

2-(β -Pyridyl)- Δ^2 -thiazoline-4-hydroxamic acid (XIII). Prepared similarly to the γ -analog, starting from 1.33 g of (X) and 0.42 g of hydroxylamine hydrochloride. Yield 1.02 g (76.7%). M.p. 172-173° (decomp.) (from 85% alcohol). Fine, colorless prisms, very difficultly soluble in water, alcohol, and chloroform, insoluble in ether and ethyl acetate.

Found %: C 48.65; H 4.21; N 18.44; S 14.59. $C_8H_9O_2N_3S$. Calculated %: C 48.42; H 4.07; N 18.82; S 14.36.

2-(β -Pyridyl)- Δ^2 -thiazoline-4-carboxylic acid hydrazide (XIV). The procedure was the same as for the γ -pyridyl derivative, starting from 1.11 g of ester (X) and 0.34 ml of hydrazine hydrate. Yield quantitative. M.p. 161-162° (decomp.) (from 80% alcohol). Colorless needles, sparingly soluble in water, alcohol, dioxane, and ethyl acetate, insoluble in ether and benzene.

Found %: C 48.58; H 4.52; N 25.21; S 14.67. $C_9H_{10}ON_4S$. Calculated %: C 48.63; H 4.53; N 25.21; S 14.42.

SUMMARY

1. Condensation of mercaptoethylamine and of β -mercaptopropylamine with γ -pyridinenitrile gave 2-(γ -pyridyl)-5-methyl- Δ^2 -thiazoline.
2. Condensation of cysteine methyl ester with iminoesters of nicotinic and isonicotinic acids gave esters of 2-(β - and γ -pyridyl)- Δ^2 -thiazoline-4-carboxylic acids, from which the acids and their derivatives were prepared.

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SYNTHESES OF ISOXANTHINE DERIVATIVES

III. 1,9-DIMETHYLISOXANTHINE

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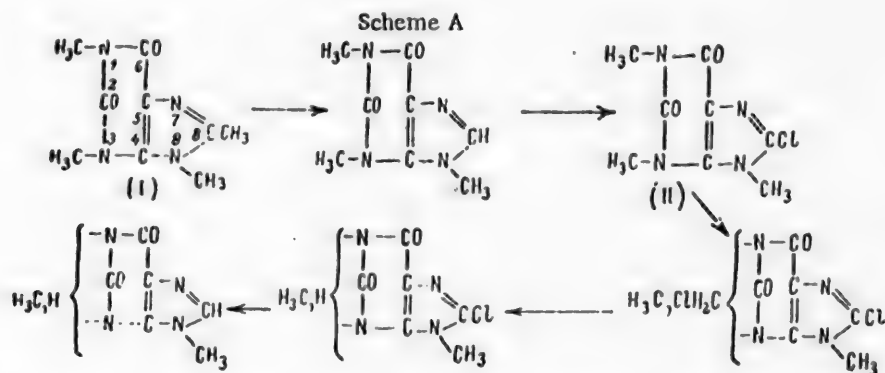
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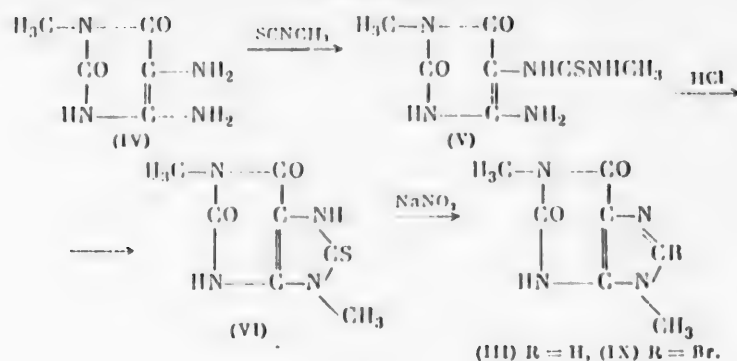
Original article submitted August 28, 1959

Preparation of dimethylisoxanthine from 1, 3, 8, 9-tetramethylisoxanthine was described in preceding communications [1, 2]. Detachment of two methyl groups from compound (I) proceeded through the step of formation of 8-chloroisocaffeine (II) [3] in accordance with the scheme:



The first objective of the present work was to conclusively establish the positions of the methyl groups in the dimethylisoxanthine formed in the above reactions. One of them is undoubtedly located at N_9 which is fixed by the $\Delta^{7,8}$ in the imidazole portion of the molecule. This follows from the properties of the compound obtained, from comparison of its ultraviolet spectrum with the spectra of other isoxanthines [3], and from the results of its oxidation with potassium dichromate in sulfuric acid [4]. The last reaction leads to formation of methylparabanic acid with retention of the imidazole ring. The presence of a methyl group was confirmed by analysis. But the position of the second N-methyl group (in the pyrimidine ring) was unknown. The earlier conjecture that it was linked to N_1 and not to N_3 lacked experimental proof since it was based only on comparison of the melting point of the prepared compound (350°) with the literature data, namely with the melting points of 1,9-dimethylisoxanthine (350°) and 3,9-dimethylisoxanthine (364°) [5]. The required confirmation was obtained by syntheses of 1,9-dimethylisoxanthine (III) and its comparison with the dimethylisoxanthine obtained from compound (II). Compound (III) was synthesized by scheme B, i.e. by condensation of 1-methyl-4,5-diaminouracil (IV) with methyl thioisocyanate, cyclization of the resulting ureide (V), and desulfurization of the 1,9-dimethyl-8-thiouric acid (VI) [cf. 5, 6].

Scheme B



The 1,9-dimethylisoxanthine (III) obtained in this manner was found to be identical with the dimethylisoxanthine prepared by scheme A. The identity of the chloraurates of both compounds was also established. These data, in conjunction with the results of oxidative cleavage of the dimethylisoxanthine concerned, demonstrate that chlorine acts on compound (II) under the previously described conditions [2] with replacement by chlorine of one of the hydrogens of the methyl group at N₃ and with subsequent hydrolytic cleavage of this chloromethyl group.

The second objective of this investigation was the improvement of the method of preparation of 1,9-dimethylisoxanthine from compound (I). A study was made, in this connection, of the possibility of simultaneous removal of two methyl groups in (I) and intermediate formation of a tetrachloride, namely 8-trichloromethyl-3-monochloromethyl-1,9-dimethylisoxanthine (VII). Investigation of the replacement of four hydrogens in (I) by chlorine atoms showed that replacement of the three hydrogen atoms of the methyl group in position 8, i.e. formation of 8-trichloromethyl-1,3,9-trimethylisoxanthine (VIII), goes with very great facility if three moles of chlorine are passed into a suspension of (I) in an organic solvent heated to 95-100° [2]. Introduction of a fourth atom of chlorine into the N-methyl group of intermediate compound (VIII) requires a higher temperature and the employment of a considerable excess of chlorine. A pure tetrachloro compound with m.p. 177-178° could be isolated from the mixture resulting from such a chlorinating treatment. It was hydrolyzed with water with loss of four equivalents of HCl and one equivalent of formaldehyde to form a dimethylisoxanthine identical with the 1,9-dimethylisoxanthine previously obtained by schemes A and B.* It was established in this manner that, instead of the accepted conversion of methylcaffeine into theophylline [7], the fourth chlorine atom enters not in the imidazole ring but in the N-methyl group of the pyrimidine ring in position 3.

The tetrachloro derivative (VII), which can also be prepared by the action of chlorine on pure 8-trichloromethylisocaffeine (VIII), is extremely soluble in organic solvents, its solubility approaching that of other chloro derivatives (I); its separation from the mixture of chloro derivatives is therefore associated with serious losses. By contrast, the product of its hydrolysis—1,9-dimethylisoxanthine (III)—differs markedly from the other products of hydrolysis by virtue of its poor solubility in water, its ability to dissolve in caustic alkalis and to separate from alkaline solutions on acidification, its low basicity, and other properties. These differences permitted the development of a method of preparation of (III) based on chlorination of (I) in chlorobenzene at 120° with excess of chlorine (7-8 moles instead of 4) and subsequent hydrolysis of the total chlorinated substances. Compound (III) separates from the resultant mixture at pH 1-3, i.e. when the remaining (more highly basic) products are retained in solution as hydrochlorides. This simplified method of preparation of 1,9-dimethylisoxanthine (scheme C) excludes the separation of intermediate substances (VII) and (VIII). With its smaller number of steps it has undoubted advantages over the previously described scheme A [3].

*The components of the difficultly separable mixture of chlorinated compounds generally do not depress the melting points of one another. The purity of the tetrachloro derivative with m.p. 177-178° was confirmed by analysis, by titration of the solution resulting from hydrolysis of a weighed sample, and by quantitative determination of the formaldehyde thereby formed.

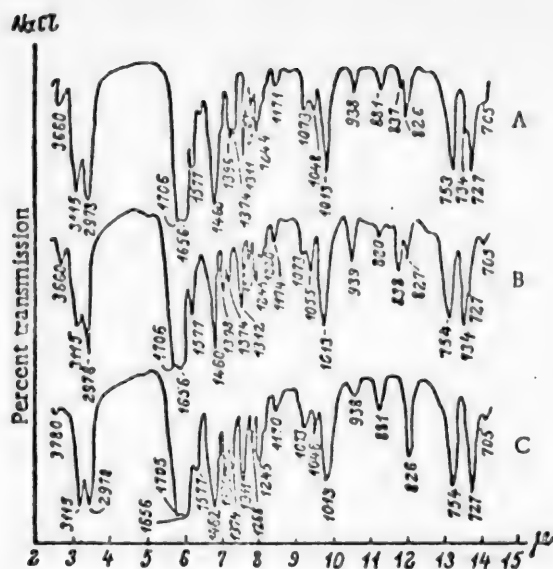


Fig. 1. Infrared spectra of 1,9-dimethylisoxanthine obtained by schemes A, B, and C.

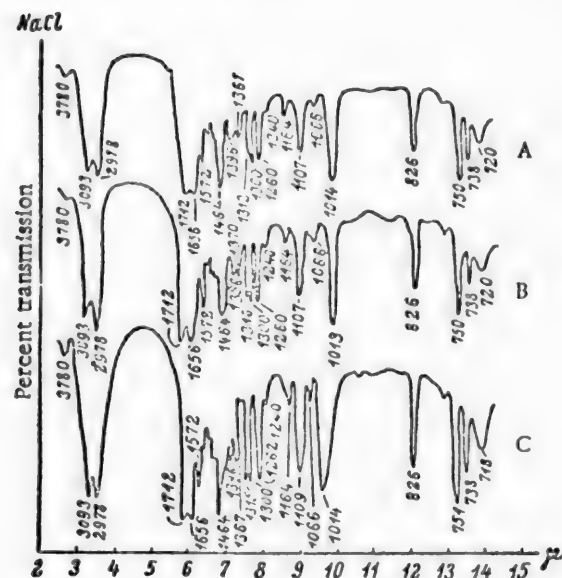


Fig. 2. Infrared spectra of the bromo derivative of 1,9-dimethylisoxanthine prepared by schemes A, B, and C.

Found %: N 30.67. $C_7H_{11}O_2N_5S$. Calculated %: N 31.11.

8-Trichloromethyl-1,9-dimethyl-3-monochloromethylisoxanthine (VII). a) From 1,3,8,9-tetramethylisoxanthine (I). Excess of dry chlorine (~10 g) was passed through a stirred suspension of 5 g of (I) [1] in 100 ml

The identity of the dimethylisoxanthine obtained from (I) by schemes A and C with the 1,9-dimethylisoxanthine synthesized by scheme B was further confirmed by comparison of their infrared spectra (Fig. 1) as well as by bromination of the three samples of dimethylisoxanthine by bromine in glacial acetic acid. This bromination led in all cases to formation of one and the same compound (IX) — 8-bromo-1,9-dimethylisoxanthine. This was confirmed by determination of the melting points of mixed specimens and by comparison of the infrared spectra (Fig. 2) of the products of bromination. The location of the bromine at C₈ is established in the next communication in this series.

EXPERIMENTAL

1-Methyl-4-amino-5-(3'-methylthioureido) - uracil (V). A mixture of 6.4 g of 1-methyl-4,5-diaminouracil, 3.24 g of $SCNCH_3$, and 45 ml of alcohol was stirred at the boil for 6 hr. The filtered precipitate was washed and used in the cyclization reaction without purification; yield 8 g. It was crystallized twice from water before analysis.

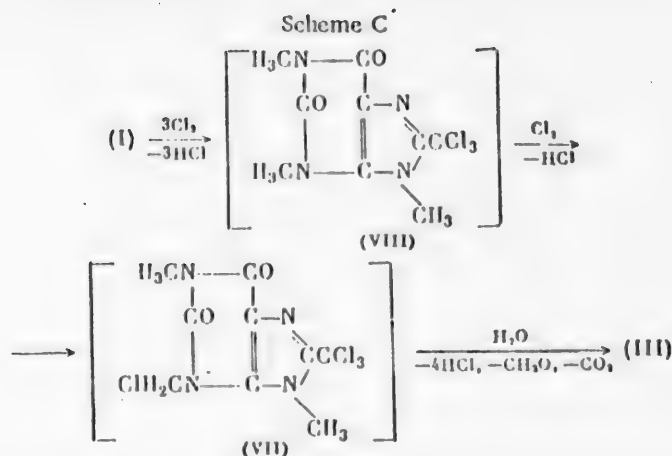
Found %: N 30.72. $C_7H_{11}O_2N_5S$. Calculated %: N 30.57.

1,9-Dimethyl-8-thiouric acid (VI). A mixture of 6.6 g of (V) and 60 ml of concentrated hydrochloric acid was boiled for an hour, cooled, and filtered. The crystalline precipitate was washed with hydrochloric acid, water, and alcohol; yield 5.6 g [5]. The crystals were crystallized twice from water before analysis.

Found %: N 26.17. $C_7H_8O_2N_4S$. Calculated %: N 26.41.

1,9-Dimethyl- $\Delta^{7,8}$ -isoxanthine (III). In the course of 3 hr 13.5 g of sodium nitrite was added in small portions with energetic stirring to a mixture of 5.2 g of (VI) and 21 ml of 6 N hydrochloric acid. Warm water (50 ml) and a little hydrochloric acid were added after 2 hours' stirring. The filtered solution was neutralized with ammonia to pH 4-4.5, and the precipitate was collected (4.1 g) and crystallized from 250 ml of water. Yield 3 g of (III) with m.p. 337-338° (decomp.). After three crystallizations the compound melted at 350-350.5° (decomp.). For analysis it was dried at 130°.

*1-Methyl-4,5-diaminouracil was prepared from 1-methyl-4-amino-5-isonitrosouracil by reduction with sodium hydrosulfite in formamide with addition of formic acid [8] or by treatment with zinc dust in 50% formic acid [9] followed by hydrolysis of the resulting 1-methyl-4-amino-5-formylaminouracil. The authors are extremely grateful to K. A. Chkhikvadze who kindly supplied the 1-methyl-4-aminouracil. We also thank Yu N. Shelinker and his colleagues for examining the infrared spectra of our preparations.



of dry chlorobenzene heated to 118-120°; the solid gradually went into solution and heating was continued at the same temperature for an hour. The excess of chlorine was purged out by a stream of dry air and the chlorobenzene was distilled in vacuo (temperature not above 80°, volume of residue ~ 10 ml). After cooling, the yellow crystals were suction-filtered and washed with cold benzene. The solid (weight 6.37 g, m.p. 182-184°) was then boiled with 20 ml of benzene and filtered hot [0.58 g of impure (VIII) with m.p. 193-194° • did not dissolve]; the filtrate deposited 5.28 g of crystals with m.p. 184-186°, consisting of compound (VII) with a small admixture of product (VIII). This impurity could be separated by crystallization from ethyl acetate, in which (VIII) is less soluble than (VII), or from chloroform. In the latter case compound (VIII) is retained in the mother liquor. Numerous purifications yielded pure (VII) with m.p. 177-178°.

Stout, transparent prisms, solubility at the boil in chloroform 1:12, in trichloroethylene 1:24, in ethyl acetate 1:10, in benzene 1:6. Crystallizes from benzene with two moles of solvent.

Found %: C 31.40; H 2.5; Cl 40.94; N 15.93; $\text{C}_9\text{H}_4\text{O}_2\text{N}_4\text{Cl}_4$. Calculated %: C 31.21; H 2.6; Cl 41.04; N 16.18;

A mixture of 0.3721 g of pure (VII) and 2 ml of water was boiled for 3 hr. The solution was neutralized to Methyl Orange with 1 N NaOH; the consumption of alkali was equivalent to 4 moles of HCl. Cooling led to separation of 0.1849 g (95.5%) of 1,9-dimethylisoxanthine with m.p. 350-352° (decomp.). A mixture with (III) prepared from (VI) melted at 350-352° (decomp.).

b) From 8-trichloromethyl-1,3,9-trimethylisoxanthine (VIII). A mixture of 5 g of (VIII) [2] and a solution of 1.45 g of chlorine in 16 ml of POCl_3 was heated for 14 hr in a tube at 100°, the POCl_3 was distilled off, and the residue treated with ether. The crystalline product (weight 3.64 g, m.p. 144-154° with decomp.) was twice crystallized from ethyl acetate. Yield 1.69 g with m.p. 172-176°, rising to 176-178° after recrystallization. A mixture with compound (VII) prepared by method a) melted at 176-178°.

c) In the course of 1.5 hr excess of dry chlorine (~ 4 g) was passed into 5 g of (VIII) in 70 ml of dry chlorobenzene heated to 115-120°; heating was continued for another hour at the same temperature, the excess of chlorine was purged out by a stream of dry air, the chlorobenzene was distilled off in vacuo, the residue (5-7 ml) was cooled, and the crystals suction-filtered (weight 3.75, m.p. 176-177°). A mixture with pure product (VII) melted at 176-178°. After recrystallization from ethyl acetate the m.p. was 177-178°.

Found %: Cl 41.43; N 16.25; $\text{C}_9\text{H}_4\text{O}_2\text{N}_4\text{Cl}_4$. Calculated %: Cl 41.04; N 16.18.

After 2.2839 g of substance with m.p. 176-177° had been boiled with 10 ml of water for 3 hr, the solution was neutralized with 1 N NaOH solution in presence of Methyl Orange; neutralization consumed 96% of the calculated quantity of alkali. Compound (III) came down; weight 0.6664 g (56.2%), m.p. 348-350° (decomp.). A mixture with compound (III) prepared from compound (II) [3] melted at 348-351° (decomp.).

1,9-Dimethylisoxanthine (III). In the course of 5 hr 248 g of dry chlorine was passed into a suspension of 104 g of dry (I) in 1000 ml of dry chlorobenzene at 118-120°. At first a fast stream of chlorine was admitted, but

• A mixed sample of pure (VII) with m.p. 177-178° and (VIII) with m.p. 214.5-215° (1:1) melted at 193-194°.

after completion of dissolution (~ 1 hr) it was slowed down. Crystals came out on cooling and were collected (weight 93 g, m.p. 137-143°), and the filtrate was concentrated to a small volume in vacuo at -70° and cooled. After 3-4 hr, the crystallized mass was filtered to give an additional 62 g of substance with m.p. 135-140°. The total unpurified compound (VII) (155 g) was boiled for 3 hr with 800 ml of water, decolorized with carbon, and cooled. The solution was neutralized and white crystals came down from the solution at pH 3; weight 52.6 g, m.p. 337-338° (decomp.). Crystallization from 2300 ml of water gave 37.75 g with m.p. 347.5-348° (decomp.).

Evaporation of the aqueous mother liquors gave an additional 3 g with m.p. 347-348° (decomp.). Total yield of compound (III) 40.75 g (45.3%). Mixtures with compound (III) prepared by schemes A [3] and B melted at 347-348° (decomp.).

For analysis the compound was crystallized twice from water and dried at 130° to constant weight. Fine, small, white needles with m.p. 350-351° (decomp.).

Found %: C 46.36; H 4.92; N 30.8; $C_7H_9O_2N_4$. Calculated %: C 46.66; H 4.44; N 31.11.

Oxidation of 1,9-dimethylisoxanthine (III). Preparation of methylparabanic acid. A mixture of 4 g of (III), a solution of 7.1 g of $K_2Cr_2O_7$, and 9.35 g of conc. H_2SO_4 in 75 ml of water was boiled for 5 hr; the cooled reaction mass was extracted several times with ether; weight of residue after evaporation of the ether 0.85 g, m.p. 150-152°, rising to 152.5-153.5° after crystallization from water. Literature [4]; m.p. 151°.

Found %: N 21.49. $C_4H_4O_3N_2$. Calculated %: N 21.87.

The ether-extracted aqueous solution was neutralized to pH 7 and evaporated to dryness. Ether extraction of the dry residue yielded a further 0.9 g of substance with an unsharp melting point and melting at 145-147° after crystallization from water.

Chloroaurate of compound (III). Addition of 0.5 ml of 15% $HAuCl_4$ solution to a solution of 0.05 g of (III), prepared by scheme A, in 1 ml of concentrated hydrochloric acid led to deposition of 0.11 g of salt in the form of yellow needles; m.p. 250° (decomp.).*

Chloroaurates prepared from compound (III) synthesized by methods B and C have the same crystal form (needles) and melt at 250° (decomp.). Mixed samples melt at 250° (decomp.).

8-Bromo-1,9-dimethylisoxanthine (IX). To a suspension of 3 g of (III), prepared by scheme A, in 60 ml of boiling glacial acetic acid was slowly added 3 ml of bromine. A voluminous, dark-red precipitate came down from the transparent solution formed after addition of the first drops of bromine; its color gradually changed to bright yellow. After the whole of the bromine had been added, the precipitate was separated and washed with acetic acid and alcohol; weight 4.2 g, m.p. 265-266.5° (decomp.). Crystallization from 700 parts of boiling water gave colorless, elongated rhombs with m.p. 277-278° (decomp.).

Found %: C 32.58; H 2.84; Br 31.05. $C_7H_7O_2N_4Br$. Calculated %: C 32.43; H 2.70; Br 30.89.

The reaction leading from substance (III) prepared by scheme B to 8-bromo-1,9-dimethylisoxanthine is identical with the reaction starting from (III) prepared by scheme C. The Br contents of the respective products are 31.01 and 30.84%. A mixed sample melts at 277-278°.

SUMMARY

1. Reaction of 8-trichloromethyl-1,3,9-trimethylisoxanthine with excess of chlorine leads to replacement by chlorine of one of the hydrogen atoms at N_3 ; hydrolysis of the resulting 8-trichloromethyl-1,9-dimethyl-3-monochloromethylisoxanthine leads to detachment of two chloromethyl groups (at N_3 and C_9) with formation of 1,9-dimethylisoxanthine identical with the 1,9-dimethylisoxanthine synthesized for comparison from 1-methyl-4,5-diaminouracil and methyl thioisocyanate.

2. The method of preparation of 1,9-dimethylisoxanthine from 1,3,8,9-tetramethylisoxanthine through the step of formation of 8-trichloromethyl-1,9-dimethyl-3-monochloromethylisoxanthine was simplified by chlorination of 1,3,8,9-tetramethylisoxanthine with excess of chlorine and hydrolysis of the chlorination product without separation of intermediates.

* M.p. 255° (decomp.) is reported [5] for the chloroaurate of 1,9-dimethylisoxanthine. The same source also mentions the acicular shape of the crystals. The chloroaurate of 3,9-dimethylisoxanthine has also been described; its melting point [5] is given as 297-300° (decomp.) and it is said to crystallize in clusters of fine, microscopic crystals.

3. Dimethylisoxanthine, previously obtained by demethylation of 1,3,8,9-tetramethylisoxanthine via the step of formation of 8-chloro-1,3,9-trimethylisoxanthine, is identified as 1,9-dimethylisoxanthine.

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SYNTHESES OF ISOXANTHINE DERIVATIVES

IV. 8-ALKOXY DERIVATIVES OF 1,9-DIMETHYL- AND 1,3,9-TRIMETHYLISOXANTHINE

I. M. Ovcharova and E. S. Golovchinskaya

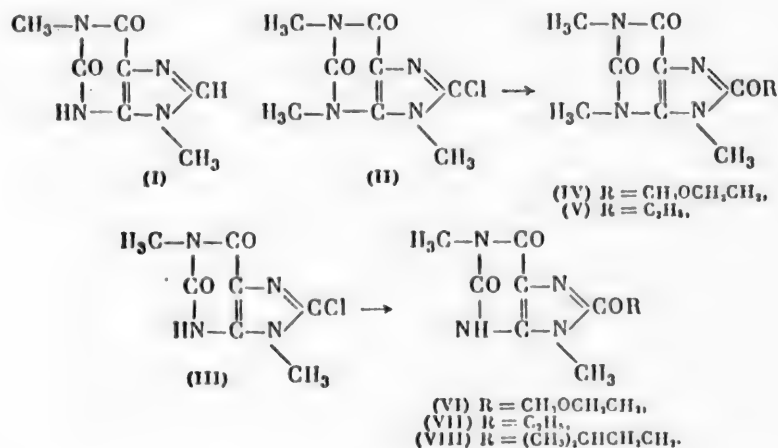
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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10, pp. 3339-3343,

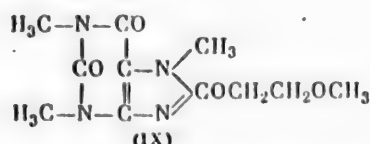
October, 1960

Original article submitted August 28, 1959

The present paper describes the synthesis of some 8-alkoxy derivatives of isocaffeine (1,3,9-trimethylisoxanthine) and of 1,9-dimethylisoxanthine (I). The starting substances for synthesis of these compounds were the previously described 8-halo derivatives of methylated isoxanthines [1, 2] and in particular 8-chloroisocaffeine (II) and 8-chloro-1,9-dimethylisoxanthine (III).



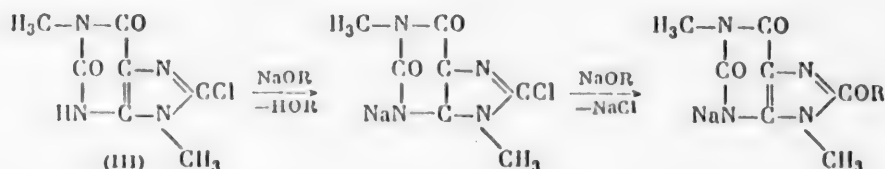
The synthesis of 8-(2'-methoxyethoxy)isocaffeine (IV) and 8-(2'-methoxyethoxy)-1,9-dimethylisoxanthine (VI) was prompted by the announcement of the physiological activity of 8-(2'-methoxyethoxy)-caffeine (IX) [3].



In addition to these two compounds, we synthesized 8-ethoxyisocaffeine (V), 8-ethoxy-, and 8-isoamyloxy-1,9-dimethylisoxanthine (VII, VIII).

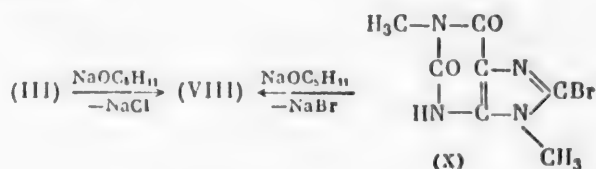
Compounds (V) and (IV) are formed with relative facility when 8-chloroisocaffeine (II) is boiled with one mole of NaOC_2H_5 in anhydrous alcohol and with 1 mole of $\text{NaOCH}_2\text{CH}_2\text{OCH}_3$ in α -hydroxy- β -methoxyethane

respectively. In the case of 8-chloro-1,9-dimethylisoxanthine (III), this replacement of halogen by an alkoxy group requires the use of two moles of alkoxide since one mole is at once consumed in formation of the sodium salt (which is relatively poorly soluble in alcohols) due to the presence of the unsubstituted hydrogen at the nitrogen.

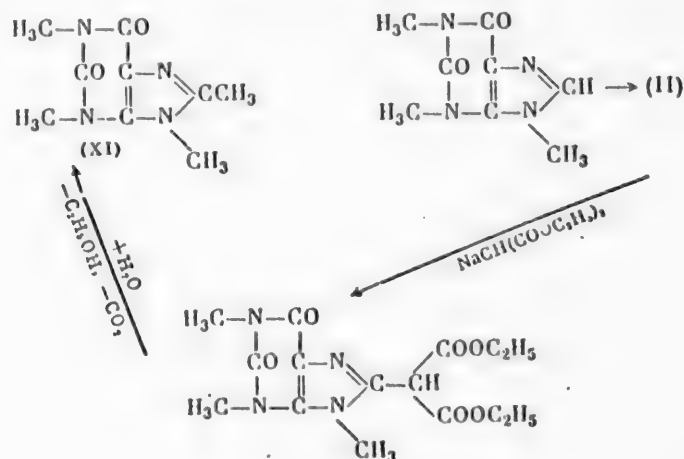


A higher temperature is also necessary in this case. Reaction of (II) with sodium ethoxide takes place even at the boiling point of alcohol, but (III) enters into the analogous reaction only at 120°. A necessary condition for reaction of the sodium salt of (III) with alkoxides is its ability to dissolve in the reaction medium; boiling of the dry salt of substance (III) with dry ethoxide in xylene led to quantitative recovery of the starting components.

Compound (VIII) was prepared from two starting substances: from substance (III) and from the monobromo derivative of 1,9-dimethylisoxanthine (X); the latter had previously been obtained by the action of molecular bromine on 1,9-dimethylisoxanthine [2].



These two parallel reactions were performed in order to confirm the structure of this bromo derivative. Formation of the identical substance from it and from compound (III) in reaction with sodium isoamyloxyde showed that the action of bromine on 1,9-dimethylisoxanthine results in replacement of the hydrogen at C₈ and not at any other position in the molecule. It also showed in turn that the bromine-containing compound is indeed 8-bromo-1,9-dimethylisoxanthine [2]. This conclusion is fully supported by the fact that the location of the chlorine at C₈ in the molecule of (III) is beyond dispute [(III) is converted to 8-chloroisocaffeine (II) on methylation with diazomethane]; its structure is also determined by its synthesis from (II) [1]; finally the position of the chlorine has been conclusively established by conversion of the compound to the well-known methylisocaffeine (XI) by the following reactions, i.e. by condensation of (II) with sodium malonic ester followed by hydrolysis and decarboxylation of the product of condensation.



Doubt about the position of the bromine at C₈ in the compound obtained by bromination of (I) arose because attempts to prepare the already known compound (III) [1] by a similar route (i.e. by the action of molecular chlorine on 1,9-dimethylisoxanthine (I)) were unsuccessful. This transformation, i.e. direct chlorination of (I), has nevertheless now been effected by reaction of (I) with sulfonyl chloride.

The sodium salts of compounds (VI), (VII), (VIII), and (I), as well as the previously described sodium salt of (III) [1], can be recrystallized from water in which they are moderately soluble without heating. Their potassium salts are rather more soluble but their solubility is likewise poor.

EXPERIMENTAL

8-(2'-Methoxyethoxy)-isocaffeine (IV). A solution of 0.53 g of sodium in 45 g of α -hydroxy- β -methoxyethane was boiled with 5.3 g of 8-chloroisocaffeine for 27 hr. After partial removal of solvent in vacuo, the residue crystallized and was filtered and washed with ether; weight 5.7 g. After crystallization from 170 ml of alcohol, the yield of compound (IV) was 1.6 g; long needles, m.p. 221-222°; one part is soluble in 15 parts of boiling water. For analysis it was crystallized from 45 parts of alcohol.

Found %: N 20.85. C₁₁H₁₆O₄N₄. Calculated %: N 20.89.

8-Ethoxyisocaffeine (V). A solution of 1 g of sodium in 350 ml of anhydrous alcohol was boiled with 10 g of 8-chloroisocaffeine for 24 hr (until the alkaline reaction to phenolphthalein disappeared). The cooled reaction mass was dissolved in water and filtered; weight 5.8 g, m.p. 238-239°. Concentration of the filtrate led to isolation of an additional 2.5 g of crystals with m.p. 238-240°. After two recrystallizations from water (1:170) the product weighed 3.8 g; m.p. 260.5-261°. Evaporation of part of the water from the crystallization mother liquors gave an additional 1.3 g of substance with m.p. 260.5-261°. Total yield of compound (V) 5.1 g (49%). Colorless, elongated plates; solubility in boiling alcohol 1:85.

Found %: N 23.33; C₉H₉O 19.18. C₁₀H₁₄O₃N₄. Calculated %: N 23.53; C₉H₉O 18.91.

8-(2'-Methoxyethoxy)-1,9-dimethylisoxanthine (VI). A solution of 0.43 g of sodium in 30 g of α -hydroxy- β -methoxyethane was boiled with 2 g of 8-chloro-1,9-dimethylisoxanthine for 25 hr with stirring. The precipitated sodium chloride was removed by filtration, and the excess of α -hydroxy- β -methoxyethane taken off in vacuo. Yield 2.7 g of sodium salt of (VI). The salt was dissolved in 12 ml of water and the solution acidified with 40% H₂SO₄ to pH 5. The precipitate (2 g, m.p. 250-252°) was crystallized from water. Yield 1.45 g (61.5%). Long, colorless prisms, m.p. 254-255°.

Found %: N 22.10. C₁₀H₁₄O₄N₄. Calculated %: N 22.04.

Sodium salt of 8-(2'-methoxyethoxy)-1,9-dimethylisoxanthine. The sodium salt was precipitated from a filtered solution of 2.2 g of (VI) in 4 ml of 2 N NaOH solution by addition of 200 ml of acetone. The filtered precipitate was washed with acetone. Yield 2.25 g, decomp. p. ~ 330°. The sodium salt of (VI) has good solubility in water, as well as in ethyl and methyl alcohols. It is insoluble in acetone. It crystallizes from water with two moles of water (drying at 130° gives a weight loss of 11.85%).

Found %: N 18.21. C₁₀H₁₃O₄N₄Na·2H₂O. Calculated %: N 17.99.

8-Ethoxy-1,9-dimethylisoxanthine (VII). A solution of 0.215 g of sodium in 15 ml of anhydrous alcohol was heated with 1 g of 8-chloro-1,9-dimethylisoxanthine in an autoclave at 120-130° for 28 hr, the alcohol was taken off in vacuo, and the residue crystallized from 210 ml of water. Yield of (VII) 0.58 g (55.7%). Colorless, elongated plates, m.p. 261-262° (decomp.), solubility in boiling alcohol 1:260, in boiling water 1:300.

Found %: N 24.84. C₉H₁₂O₃N₄. Calculated %: N 25.00.

8-Isoamyl-1,9-dimethylisoxanthine (VIII). a) From 8-chloro-1,9-dimethylisoxanthine (III). A solution of 2.14 g of sodium in 200 ml of anhydrous isoamyl alcohol was boiled with 10 g of 8-chloro-1,9-dimethylisoxanthine for 22 hr. The reaction mass was shaken with water, and the aqueous layer separated and acidified with 40% H₂SO₄ to pH 4. Acidification led to separation of 10.3 g of substance which was boiled with 200 ml of water. The resulting suspension was filtered hot. The filtrate deposited 1 g of unreacted starting compound (III) with m.p. 295° (decomp.). The water-insoluble precipitate (8.9 g, m.p. 245°) was twice crystallized from isoamyl alcohol (1:45) to give 5.3 g of colorless, elongated plates with m.p. 251-252° (decomp.). Concentration of the mother liquors yielded a further 1.3 g with m.p. 250-251° (decomp.). Total yield of (VIII) 6.6 g (53.6%).

Found %: N 21.01. $C_{12}H_{13}O_3N_4$. Calculated %: N 21.05.

b) From 8-bromo-1,9-dimethylisoxanthine. A solution of 0.215 g of sodium in 35 ml of anhydrous isoamyl alcohol was boiled for 22 hr with 1 g of 8-bromo-1,9-dimethylisoxanthine. The reaction mass was worked up as in a) to give 0.6 g of substance (VIII) with m.p. 251-252° (decomp.). A mixture with (VIII) from expt. a) melted at the same temperature.

Sodium salt of 8-isoamyloxy-1,9-dimethylisoxanthine. Stirring of 3 g of (VIII) in 6 ml of 2 N NaOH solution led to formation of a viscous mass which went into solution after heating with 21 ml of water. Crystals came out on cooling. Yield 2.55 g of sodium salt in the form of fine needles with m.p. ~ 290° (decomp.); the salt had a solubility in water at 25° of 1.25; it was readily soluble in alcohol, and insoluble in acetone, ether, and other organic solvents. For analysis it was crystallized from boiling water (1:6). It crystallizes with 2 moles of water (at 130° the weight loss is 11.38%).

Found %: N 17.72. $C_{12}H_{17}O_3N_4Na \cdot 2H_2O$. Calculated %: N 17.3.

Sodium salt of 1,9-dimethylisoxanthine. The salt came down from a filtered solution of 5 g of (I) in 55 ml of 0.5 N NaOH solution after addition of 15 ml of alcohol. Yield 4.1 g of product in the form of white needles with m.p. (decomp.) 359-361°. For analysis it was crystallized from 115 parts of alcohol. It crystallizes with 2 moles of water (the weight loss after drying at 140° is 15.06%).

Found %: N 23.44. $C_7H_7O_2N_4Na \cdot 2H_2O$. Calculated %: N 23.53.

8-Chloro-1,9-dimethylisoxanthine (III). 1,9-Dimethylisoxanthine (10 g) was stirred with distilled SO_2Cl_2 (65 ml) at room temperature for ~ 100 hr. The reaction mass was filtered. The precipitate was washed with dry dichloroethane, then suspended in 30 ml of ice water, and filtered. There was obtained 8.9 g of product with m.p. 299-300° (decomp.); after crystallization from water the yield of (III) was 7 g (58.8%) with m.p. 316-317° (decomp.). A mixture with (III) obtained from 8-chloroisocaffeine [1] melted at the same temperature. Neutralization with caustic alkali of the acid aqueous filtrate from the unpurified compound (III) to pH 5 gave 0.4-0.5 g of unreacted 1,9-dimethylisoxanthine (I).

SUMMARY

1. Some 8-alkoxy derivatives of 1,9-dimethyl- and 1,3,9-trimethylisoxanthine were synthesized.
2. Reaction of 1,9-dimethylisoxanthine with sulfuryl chloride gave 8-chloro-1,9-dimethylisoxanthine. The product was identical with the substance previously obtained by demethylation of 8-chloro-1,3,9-trimethylisoxanthine.

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* Original Russian pagination. See C. B. translation.

DERIVATIVES OF DIACETYL-m-PHENYLENEDIAMINE CONTAINING QUATERNARY AMMONIUM GROUPS IN THE ACETYL RADICALS

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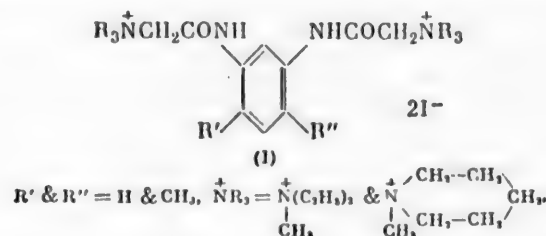
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October, 1960

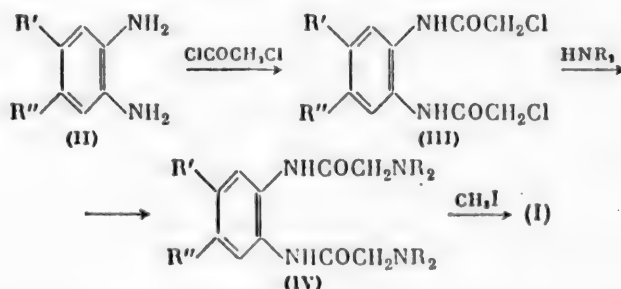
Original article submitted November 12, 1959

Bis-quaternary ammonium compounds possess high pharmacological activity in the majority of cases. A series of investigations has shown that the nature of the pharmacological activity and the degree of activity of such compounds depends in great measure on the length of the chain linking the two quaternary ammonium groups [1-4]. Very much less work has been carried out on the influence of the alkyl radicals present both in the ammonium groups and in the central part of the molecule on the pharmacological properties of bis-quaternary ammonium compounds (see [5-7]).

In the present work we describe the synthesis of a series of compounds with the general formula (I).

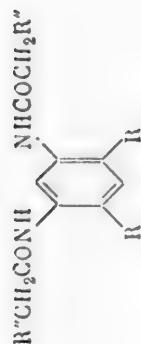


The starting diamines were m-phenylenediamine, 4-methyl-m-phenylenediamine, and 4,6-dimethyl-m-phenylenediamine. Compound (I) was synthesized by the following route:



Conversion of (II) into (III) was effected by reaction of the diamine with chloroacetyl chloride in acetic acid solution. Heating of (III) with diethylamine or piperidine gave products (IV) which on reaction with CH_3I gave the corresponding bis-quaternary ammonium salts (I). All of the synthesized compounds are forth in the table.*

*Pharmacological tests on the preparations were undertaken by A. I. Podlesnaya and N. K. Frumentov to whom we express our profound thanks. For results of these tests see the summary.



Prep. no.	R	R'	R''	Melting point	Boiling point (pressure in mm)	Yield (%)	Empirical formula	Found (%)			Calculated (%)		
								C	H	N	C	H	N
1	H	H	Cl	228-230°	—	78	C ₁₀ H ₁₀ N ₂ O ₂ Cl ₂	45.75	3.78	10.73	45.99	3.68	10.73
2	H	H	N(C ₂ H ₅) ₂	—	216-217° (1)	55	C ₁₈ H ₃₀ N ₄ O ₂	64.28	10.12	16.62	64.64	9.04	16.75
3	H	H	N(C ₂ H ₅) ₂ CH ₃ · I-	198-202	—	79	C ₂₀ H ₃₆ N ₄ O ₂ I ₂	—	—	8.93	—	—	9.06
4	H	H	NC ₃ H ₁₀	121-124.5	—	95	C ₂₀ H ₃₆ N ₄ O ₂	66.82	8.62	15.78	67.01	8.44	15.63
5	H	H	N(C ₂ H ₅) ₂ CH ₃ · I-	156-163	—	46	C ₂₂ H ₃₆ N ₄ O ₂ I ₂	—	—	8.57	—	—	8.72
6	H	CH ₃	Cl	223-224	—	86	C ₁₁ H ₁₂ N ₂ O ₂ Cl ₂	47.82	4.51	10.26	48.01	4.39	10.18
7	H	CH ₃	N(C ₂ H ₅) ₂	—	238-243 (1.5)	82	C ₁₉ H ₃₂ N ₄ O ₂	65.72	9.47	16.21	65.48	9.26	16.08
8	H	CH ₃	N(C ₂ H ₅) ₂ CH ₃ · I-	64-69	—	70	C ₂₁ H ₃₈ N ₄ O ₂ I ₂	—	—	8.76	—	—	8.86
9	H	CH ₃	NC ₃ H ₁₀	108-110	—	82	C ₂₁ H ₃₂ N ₄ O ₂	67.49	9.00	15.21	67.71	8.66	15.04
10	H	CH ₃	N(C ₂ H ₅) ₂ CH ₃ · I-	45-50	—	82	C ₂₃ H ₃₈ N ₄ O ₂ I ₂	—	—	8.20	—	—	8.53
11	CH ₃	CH ₃	Cl	209-212	—	85	C ₁₂ H ₁₄ N ₂ O ₂ Cl ₂	49.68	5.19	9.64	49.84	4.86	9.69
12	CH ₃	CH ₃	N(C ₂ H ₅) ₂	—	230 (1.5)	91	C ₂₀ H ₃₁ N ₄ O ₂	66.02	9.18	15.65	66.26	9.45	15.46
13	CH ₃	CH ₃	N(C ₂ H ₅) ₂ CH ₃ · I-	50-53	—	48	C ₂₂ H ₄₀ N ₄ O ₂ I ₂	—	—	8.40	—	—	8.67
14	CH ₃	CH ₃	NC ₃ H ₁₀	171-172	—	92	C ₂₂ H ₃₄ N ₄ O ₂	68.63	8.51	14.19	68.36	8.86	14.50
15	CH ₃	CH ₃	N(C ₂ H ₅) ₂ CH ₃ · I-	227-231	—	77	C ₂₄ H ₄₀ N ₄ O ₂ I ₂	—	—	8.48	—	—	8.36

EXPERIMENTAL

1. Preparation of amides of monochloroacetic acid. A solution of 5 g of *m*-phenylenediamine in 60 ml of glacial acetic acid was cooled to 10° and 7.72 ml of chloroacetyl chloride was added, followed by a solution of 15.3 g of $\text{CH}_3\text{COONa} \cdot 3\text{H}_2\text{O}$ in 60 ml of water. The reaction mixture was stirred for 30 min. The resulting precipitate was filtered, washed with water several times, dried, and recrystallized from alcohol. M.p. 228-230° after three recrystallizations. The literature [6] reports m.p. 215-217°; this is the melting point of the crude product.

The dichloroacetyl derivatives of 4-methyl-*m*-phenylenediamine and 4,6-dimethyl-*m*-phenylenediamine were prepared by the same method. Yields and melting points are set forth in the table.

2. Amination of amides of monochloroacetic acid. Into a round bottomed flask, with a reflux condenser topped by a calcium chloride tube, were charged 5 g of the dichloroacetyl derivative of *m*-phenylenediamine, 140 ml of dry benzene, and 11 ml of diethylamine. The mixture was boiled for 5 hr, the precipitated diethylamine hydrochloride was filtered off, washed with dry benzene and dried, and the benzene was distilled off. Piperidine bases were prepared by the same procedure. The piperidine base described in the literature (No. 4 in table) has m.p. 121-124.5°; the literature [6] gives m.p. 111-112°.

Bases prepared from diethylamine were distilled in vacuo; those from piperidine were recrystallized from aqueous alcohol. Yields, boiling points, and melting points are set forth in the table. Base No. 14 was purified by dissolution in dilute hydrochloric acid, extraction of the solution with ether, and treatment of the aqueous layer with ammonia. The precipitate was filtered, washed with water, recrystallized from aqueous acetone, and dried.

3. Preparation of the dimethiodides. Bases Nos. 2, 7, and 9 (table) were dissolved in dry benzene, and Nos. 4 and 12 in dry acetone. Methyl iodide was added and the mixture refluxed in a flask for 1.5 hr at 40°. The methiodides were purified as follows: No. 5 was recrystallized from the minimum quantity of water; No. 3 was twice recrystallized from acetone; No. 10 was recrystallized from absolute alcohol; No. 8 was dissolved in absolute alcohol and precipitated by ether. Methiodide No. 15 was prepared in acetone solution at room temperature. The product came down after a few hours and was filtered and washed with anhydrous acetone. Methiodide No. 13 was obtained in the form of an oil which crystallized in a vacuum-desiccator. All of the methiodides were dried in a vacuum-desiccator. Yields and melting points are given in the table.

SUMMARY

1. A series of derivatives of diacetyl-*m*-phenylenediamine containing quaternary ammonium groups in the acetyl radicals was synthesized.
2. All the synthesized compounds possess both curarelike and anticholinesterase activity.
3. The curarelike activity in this series does not alter appreciably when the diethylamino group in ammonium groupings is replaced by the piperidine residue. It is lowered appreciably when two methyl radicals are brought into the benzene ring.
4. All the synthesized compounds act more strongly on pseudocholinesterase than on true cholinesterase. This selectivity increases when methyl radicals are introduced into the benzene ring.
5. The toxicity of the synthesized compounds falls in a regular manner with introduction of methyl groups into the benzene ring. The piperidinic derivatives are slightly more toxic than the corresponding diethylamine derivatives.

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ORGANOSILICON ETHERS OF ALIPHATIC ALDOXIMES

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Organosilicon compounds containing a nitrogen atom directly linked to silicon are easily hydrolyzed with rupture of the Si-N bond [1]. It appeared of interest to synthesize compounds in which the nitrogen atom was isolated from the silicon by other elements and to investigate their resistance to hydrolysis.

Satisfactory methods have been evolved for preparation of organosilicon compounds containing a nitrogen in the organic radical [2]. On the other hand, compounds in which the silicon would be linked with nitrogen via oxygen were unknown,* although analogous organic compounds containing the >C-O-N= grouping (O-alkyl ethers of oximes and esters of nitric and nitrous acid) had been well described in the literature [3-7]. Our objective in the present work was to synthesize and to study the organosilicon esters of oximes. Alkyl ethers of oximes are known [4-7] to exist in two isomeric forms as N- and O-derivatives, ** whose formation depends mainly on the method of preparation. O-Alkyl ethers are formed predominantly when oximes are directly alkylated with alkyl iodides in presence of sodium ethoxide [3-5, 7]. However the possibility of formation of N-derivatives in small quantity side by side with the O-ethers is not excluded.

We found that trialkylchlorosilanes react with aliphatic aldoximes in presence of pyridine in accordance with the equation:



This reaction goes smoothly even at room temperature and is completed after the reaction mixture has been stirred for 4-5 hr. Yields of trialkylsilyl ethers of aldoximes are 52.5-80% (calculated on the original trialkylchlorosilane). An exception is O-trimethylsilylacetaldoxime whose yield is only 22.1%. Pyridine hydrochloride was obtained in good yield in all experiments (60-100%) apart from the main reaction product.

The synthesized O-trialkylsilylaldoximes are mobile liquids with a faint ethereal odor, stable when kept.

Their physical constants and yields are set forth in the table.

O-trialkylsilylaldoximes distil without decomposition at atmospheric pressure; they are readily soluble in organic solvents (alcohol, ether, acetone, dioxane, benzene, ligroine), and poorly soluble in water.

Their structure was confirmed by reduction with hydrogen over platinum black and by hydrolysis; also through the infrared spectra.

Catalytic hydrogenation of $(\text{CH}_3)_3\text{SiON}=\text{CHC}_3\text{H}_7$ -n and $(\text{C}_2\text{H}_5)_3\text{SiON}=\text{CHC}_3\text{H}_7$ -iso did not give O-trialkylsilyl-N-alkylhydroxylamines as would have been expected from the equation



*Only quite recently have the extremely unstable organosilicon esters of nitrous acid been described [8].

**The possibility of stereoisomerism is not touched on in this paper.

Physical Constants and Yields of O-Trialkylsilylaldoximes $R_3SiON=CHR$

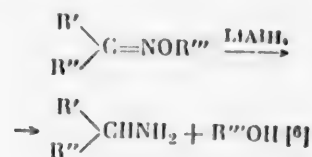
R	R'	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	M_{R_3}		M_{Si}		% Si		% N		Yield (%)
					found	calculated	found	calculated	and	calculated	found	calculated	
C_2H_5	n- C_3H_7	91.5-93 (12)	1.4375	0.8554	61.72	61.87	202.1, 203.8	201.4	13.72, 14.18	13.90	7.01, 7.16	6.95	52.5
C_2H_5	iso- C_3H_7	95 (20)	1.4325	0.8468	61.75	61.87	198.0, 197.0	201.4	13.86, 13.87	13.90	6.92, 6.71	6.95	78.0
C_2H_5	C_2H_5	86 (20)	1.4340	0.8562	56.90	57.23	184.0, 180.3	187.3	15.01, 14.96	14.97	7.32, 7.38	7.47	70.9
C_2H_5	CH_3	62-63 (13)	1.4316	0.8614	52.33	52.37	163.2, 167.6	173.3	16.20, 16.00	16.18	8.07, 8.20	8.08	79.3
CH_3	n- C_3H_7	39-41 (10)	1.4160	0.8336	47.87	47.93	155.4, 152.5	159.2	17.55, 17.60	17.61	9.10, 8.90	8.79	60.8
CH_3	iso- C_3H_7	41.5-42 (16)	1.4103	0.8256	47.90	47.93	155.8, 160.6	159.2	17.40, 17.51	17.61	8.73, 8.70	8.79	52.9
CH_3	C_2H_5	40 (28)	1.4102	0.8321	43.19	43.28	142.9, 146.6	145.2	19.18, 19.09	19.31	9.55, 9.80	9.65	53.6
CH_3	CH_3	28-30 (39)	1.4030	0.8333	38.36	38.63	133.4, 130.0	131.2	21.60, 21.52	21.70	10.91, 10.66	10.69	22.1

• Data of Vogel, Warwick, and Denby on bond refractions [9] were used.

•• The molecular weight was determined by cryoscopy in benzene.

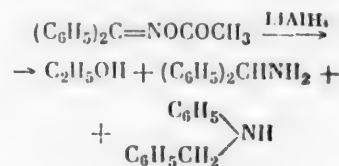
••• Silicon content determined by wet combustion.

In the hydrogenation products were found amines, ammonia, and the corresponding trialkylsilanes. Hydrogenation is consequently accompanied by rupture of the N-O bond. This is also confirmed by the amount of hydrogen absorbed being considerably larger than is required for addition to one double bond. The hydrogenation reaction consequently follows a course analogous to the reduction of O-alkyl ethers of oximes, and leads to scission of the molecule with formation of the corresponding amine and alcohol.



The primary amine in turn can undergo catalytic transformations so that a complex mixture of primary, secondary, and tertiary amines and ammonia is obtained. Reactions of this type in presence of Pd and Ni catalysts have been described by Rosenmund [10] and Vasil'ev [11].

Exner [7] also reduced o-acetylbenzophenoneoxime with $LiAlH_4$ and obtained ethyl alcohol and a mixture of primary and secondary amines.



By contrast, the reduction of N-alkyloximes in presence of $LiAlH_4$ or Pt catalyst leads smoothly to N,N-dialkylhydroxylamine [6].

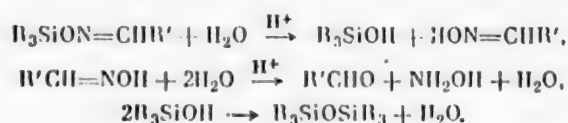
Since the hydrogenation of the trimethylsilyl ether of n-butyraldoxime and that of the triethylsilyl ether of isobutyraldoxime gave a mixture of amines and ammonia and the corresponding trialkylsilanols, we may conclude that the compounds obtained by us are the O-isomers.

A study of the hydrolysis of O-trialkylsilylaldoximes under various conditions showed that no modifications whatever occurred in the compound when $(C_2H_5)_3SiON=CHC_2H_5$ -n was subjected to vigorous and prolonged stirring with water at 20° and 60-80°. Nor does hydrolysis take place in a homogeneous aqueous dioxane medium at 20°. Replacement of water by 5% KOH solution and heating to 90° result in formation of the free oxime, although about 60% of the compound remains unchanged.

Hydrolysis of $(C_2H_5)_3SiON=CHC_2H_5$ by heating with 5% HCl proceeds with formation of aldehydes,

oximes, and nitrogen-containing resins, probably due to oxidation and condensation of the oximes and the products of their hydrolysis. Triethylsilanol is also formed and is converted into hexaethyldisiloxane (yield 53.2%).

Hydrolysis in an acid medium can accordingly be represented by the following equations:



The structure of the synthesized silyl ethers of aldoximes, as established by chemical methods, is also supported by spectral data.

The infrared spectra of all of the eight preparations contained a characteristic frequency at 1636-1640 cm^{-1} which is probably associated with the C=N valence vibrations. In aldoximes and ketoximes this corresponds to the 1630-1662 cm^{-1} frequency [12]. Vibrational data for Si—O—N bonds have not been reported in the literature; we can therefore only tentatively assign the 1050 and 850 cm^{-1} frequencies to the Si—O and O—N bond vibrations respectively in the Si—O—N system. These bands are observed in the spectra of all of the silyl ethers of aldoximes that we investigated. The bands in the 750 cm^{-1} region are probably associated with the antisymmetrical Si—C valence vibrations in the $\text{Si}(\text{CH}_3)_3$ and $\text{Si}(\text{C}_2\text{H}_5)_3$ groupings. The 1240—1250 cm^{-1} frequencies in the spectra of O-trialkylsilylaldoximes are to be assigned to the deformation vibrations, it would appear, of the $\text{Si}(\text{CH}_3)_3$ and $\text{Si}(\text{C}_2\text{H}_5)_3$ groupings [13].

EXPERIMENTAL

Starting substances. Oximes were prepared in 70—80% yields by reaction of hydroxylamine hydrochloride with the freshly distilled aldehydes.

Acetaldoxime: b.p. 114.7° (760 mm), n_D^{20} 1.4263. Literature data [14]: b.p. 115° (762 mm), n_D^{20} 1.4263; d_4^{20} 0.9640. Propionaldoxime: b.p. 130—132° (758 mm), n_D^{20} 1.4303, d_4^{20} 0.9288. Literature data [14]: b.p. 134° (761 mm), n_D^{20} 1.4303, d_4^{20} 0.9286. n-Butyaldoxime: b.p. 149—151° (760 mm), n_D^{20} 1.4362, d_4^{20} 0.9082. Literature data [14]: b.p. 151°, n_D^{20} 1.4367, d_4^{20} 0.9103. Isobutyaldoxime: b.p. 139—141° (757 mm), n_D^{20} 1.4304. Literature data [3]: b.p. 59—59.5° (20 mm), n_D^{20} 1.4302.

Trimethylchlorosilane [b.p. 58—60° (760 mm), n_D^{20} 1.3887] was prepared by rectification of the commercial product. Triethylchlorosilane with b.p. 143—145° (758 mm) and n_D^{20} 1.4309 was obtained by distillation of hexaethyldisiloxane with anhydrous aluminum chloride [15]. Pyridine, with b.p. 115—115.5° (760 mm), n_D^{20} 1.5093, d_4^{20} 1.5093, d_4^{20} 0.9824, was obtained by drying the technical product over potassium hydroxide and distilling over a small quantity of metallic sodium.

Determination of silicon content. In two experiments wet combustion was employed, and in the others the method of Sir and Komers [16]. The latter is convenient for analysis of nearly all types of organosilicon compounds. Nitrogen was determined by a microDumas technique using 2—3 crystals of Berthollet salt as catalyst.

Infrared absorption spectra were obtained with an IKS-11 apparatus with a sodium chloride prism in the 700—1700 cm^{-1} region. Thickness of layers 3, 9, and 29 μ .

Procedure for syntheses. The apparatus was a three-necked, round-bottomed flask, capacity 250 ml, fitted with stirrer, reflux condenser, and dropping funnel (the last two items had ground-glass connections). Atmospheric moisture was excluded by calcium chloride tubes. Each experiment required 0.2—0.3 mole of oxime and stoichiometric quantities of trialkylchlorosilane and pyridine. Dry benzene was the solvent. Absolute diethyl ether was the solvent for synthesis of organosilicon ethers of acetaldoxime. A mixture of benzene, oxime and pyridine was put in the flask, and benzene solution of trialkylchlorosilane was stirred in intensively. The reaction went smoothly with liberation of heat and with formation of pyridine hydrochloride. The mixture was then stirred at room temperature for 4—5 hr. The salt was suction-filtered on a Buchner funnel, washed with benzene, and dried to constant weight in vacuo. Yield of pyridine hydrochloride 95—100%. The solvent was distilled from the filtrate, and the residue twice distilled at reduced pressure through a 25-plate column. Below we give two examples of the procedure.

Synthesis of $(C_2H_5)_3SiON=CHC_3H_7$ -iso. To a solution of 34.8 g of iso- $C_3H_7CH=NOH$ in 50 ml of benzene and 32 ml of pyridine was added a solution of 60.4 g of $(C_2H_5)_3SiCl$ in 50 ml of benzene with intensive stirring and ice cooling. After 4-hours' stirring, the pyridine hydrochloride (46 g, yield 99%) was filtered off, the benzene distilled off, and the residue distilled in vacuo. Distillation gave 62.8 g (78%) of $(C_2H_5)_3SiON=CHC_3H_7$ -iso with b.p. 95° (20 mm), n_D^{20} 1.4325, d_4^{20} 0.8468.

Synthesis of $(CH_3)_3SiON=CHC_3H_7$ -n. n- $C_3H_7CH=NOH$ (29 g), $(CH_3)_3SiCl$ (36.5 g), pyridine (24 ml), and benzene (100 ml) were mixed as in the preceding example. There was obtained 38.5 g (100%) of pyridine hydrochloride.

Distillation in vacuo gave 35 g (60.8%) of $(CH_3)_3SiON=CHC_3H_7$ -n with b.p. 39–41° (10 mm), n_D^{20} 1.4160, d_4^{20} 0.8336.

Reduction of O-trimethylsilyl-n-butyraldoxime. Hydrogenation of 8.5 g of $(CH_3)_3SiON=CHC_3H_7$ -n in 30 ml of anhydrous alcohol was effected over 0.78 g freshly prepared active platinum black [17] at room temperature. During the reaction 1700 ml of hydrogen was absorbed. After completion of hydrogenation the catalyst was filtered off, the alcohol was distilled from the filtrate, and the residue was distilled to give two main fractions.

The first fraction had b.p. 77.5–99°, n_D^{20} 1.3778 (2 g). Silicon content (method of Sir and Komers [16]) 30.3 and 30.8%, indicating the presence in this fraction of a considerable proportion of $(CH_3)_3SiOH$ and $(CH_3)_6Si_2O$ [calculated for $(CH_3)_3SiOH$: Si 31.1%, for $(CH_3)_6Si_2O$ 34.5%]. Heat was released when 0.6 g of the first fraction was acetylated with acetyl chloride. Distillation gave trimethylacetoxysilane with b.p. 100–104°, n_D^{20} 1.3840; Literature data [18]: b.p. 103–104°, n_D^{20} 1.3875.

The second fraction had b.p. 157–159°, n_D^{20} 1.4198 (1.1 g). It had a sharp odor of di-n-butylamine. Determination of its content of amines by titration with 0.1 N H_2SO_4 in presence of Bromthymol blue gave a value (calculated on dibutylamine) of 88.8 and 89.5%. Literature data [20]: di-n-butylamine has b.p. 158.3–158.5° (752 mm), n_D^{20} 1.4182. The distilled alcohol contained 9.87 mg-equiv. of bases. Part of the alcohol was neutralized with hydrochloric acid and evaporated to dryness on a water bath. The separated hydrochloride melted at 197–199°. It contained 25.5% Cl and a trace of ammonium salt (faint coloration with Nessler reagent); it was evidently a mixture of the hydrochlorides of primary, secondary, and tertiary butylamines.

Reduction of O-triethylsilylisobutyraldoxime. Hydrogenation of 6.4 g of the aldoxime in 57 ml of absolute ethyl alcohol was effected over 0.64 g of platinum black at room temperature. During the reaction 1070 ml of hydrogen was absorbed. The alcoholic solution, containing 25.08 mg-equiv. of bases, was neutralized with hydrochloric acid. After distillation of the alcohol there was obtained 2.1 g of hydrochloride which was analyzed by the method of [19]. The content of volatile bases found was 7.71 mg-equiv. per gram, comprising ammonia 1.43, primary amine 3.03, secondary amine 3.13, and tertiary amine (by difference) 0.12. The distilled alcohol was redistilled from a flask surmounted by a column packed with glass rings. In this way we obtained 1.3 g of a substance with b.p. 180–230°, n_D^{20} 1.4300, d_4^{20} 0.8383. Its infrared spectrum did not contain a minimum in the 1630–1640 cm^{-1} region corresponding to the valence vibration of the C=N bond. It contained the 1086 cm^{-1} frequency characteristic of the Si-O-Si valence vibration. The compound with b.p. 180–230° is evidently hexaethyldisiloxane.

Hydrolysis of O-triethylsilyl-n-butyraldoxime. a) A mixture of 5 g of the compound and 5 ml of water was stirred at room temperature for 4 hr. No heat was liberated. The organic and aqueous layers were separated (the aqueous layer had n_D^{20} 1.3332, the organic 1.4376). Neither of the layers gave a red color with fuchsin-sulfurous acid. Similar results were obtained when hydrolysis was performed at 60–80°.

b) A mixture of 5 g of the compound and 5 g of 5% KOH solution was stirred with heating on a water bath for 4 hr. The organic layer had n_D^{20} 1.4360. After drying with calcium chloride, the organic layer was distilled in vacuo (16–17 mm). Two fractions were collected. The first (1.1 g) had b.p. 74–96°, n_D^{20} 1.4338, d_4^{20} 0.8618, and a sharp oxime odor. Some organosilicon compounds were present (large precipitate of SiO_2 on heating with a mixture of oleum and fuming nitric acid). The second (2.9 g) had b.p. 97–98°, n_D^{20} 1.4371, d_4^{20} 0.8563, corresponding to the original substance. Approximately 40% of the substance was hydrolyzed.

Hydrolysis of O-triethylsilylpropionaldoxime with 5% HCl. A mixture of 20 g of the compound and 23.5 ml of 5% HCl was stirred for 7 hr with heating on a water bath. The organic layer had n_D^{20} 1.4362. After 4-hours'

stirring, the aqueous layer contained a trace of aldehyde (red color with fuchsin-sulfurous acid). After 7-hours' stirring, the deeply colored aqueous layer was extracted with ether and evaporated to dryness. There was obtained 3.5 g of nitrogen-containing resin (positive Lassaigne reaction of nitrogen) which on treatment with FeCl_3 solution gave the deep-cherry color characteristic of hydroxamic acids. The ethereal extracts were combined with the organic layer and distilled at normal pressure. Three fractions were collected. The first had b.p. $133 - 162^\circ$ (5.1 g), n_D^{20} 1.4331. The second had b.p. $162 - 180^\circ$ (2.3 g), n_D^{20} 1.4350. The third had b.p. $220 - 229^\circ$ (7.0 g), n_D^{20} 1.4345, d_4^{20} 0.8503. Yield 53.2% (calculated on hexaethyldisiloxane).

The first and second fractions were not examined; they were evidently mixtures of propionaldoxime and starting substance. The third fraction, whose constants were close to those of hexaethyldisiloxane, was distilled with anhydrous AlCl_3 to give 8.1 g of a substance (b.p. $141.5 - 144^\circ$, n_D^{20} 1.4310) identified as triethylchlorosilane. Yield 96.3%.

SUMMARY

A preparative method of synthesis of the previously unknown O-trialkylsilyl ethers of aliphatic aldoximes was developed. Eight compounds of this type were prepared. Their structure was verified by reduction and hydrolysis reactions, and confirmed by spectral data.

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SYNTHESIS AND PROPERTIES OF TRIALKYL (TRIARYL)-(p-BROMOPHENOXY)-SILANES

I. TRIMETHYL-, TRIETHYL-, AND TRIPROPYL-(p-BROMOPHENOXY)-SILANES

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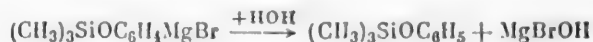
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Only the first member of the series of silicon-containing bromides of the general formula $R_3SiOC_6H_4Br$ -p, where $R = CH_3$, has been reported in the literature [1]. The objective of the present investigation was the preparation of further members of the series (with $R = C_2H_5$ and C_3H_7) and the study of the potentialities of the compounds for syntheses. The most interesting possibilities, in our opinion, were those involving the use of Grignard reagents, prepared from the bromides in question, for synthesis of silicon-containing aromatic alcohols and acids. At the same time a study was made of the resistance to hydrolysis of the ether bond ($Si-O-C_{ar}$) in these compounds.

We prepared the previously unknown triethyl- and tripropyl-(p-bromophenoxy)-silanes by catalytic dehydrocondensation of trialkylsilanes with p-bromophenol [2] in yields of 83 and 90% respectively. The trialkyl-(p-bromophenoxy)-silanes are colorless liquids, completely resistant to hydrolysis. For example, stirring for half an hour with dilute hydrochloric acid (1:10) or with 2 N NaOH did not lead to cleavage of the $Si-O-C_{ar}$ bond; 90% of the original bromides was recovered unchanged on distillation. Secondary alcohols were synthesized by the reaction:



However alcohols with $R = CH_3$ or C_2H_5 could not be obtained due to their hydrolytic instability. In the case of $R = CH_3$ the reaction products were hexamethyldisiloxane and a silicon-free resin. Alteration of the conditions for decomposition of the alcoholate (use of 1% HCl, NH_4Cl or $NaHCO_3$ solutions, pure water) had no effect on the reaction course. Preparation of hexamethyldisiloxane in 80% yield is evidence of the formation of alcoholate in good yield. Further experiments showed that disiloxane is not formed at all when the Grignard reagent is decomposed with water; in this case the reaction goes by the usual route with formation of $(CH_3)_3SiOC_6H_5$.



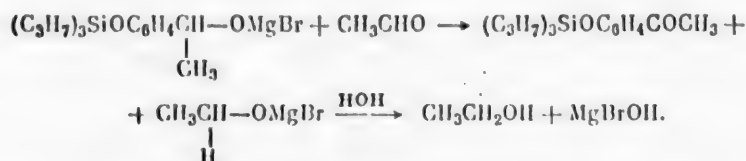
Since formation of trimethylphenoxysilane was not observed in the attempt to synthesize the alcohol, we may infer that the alcohol is not resistant to hydrolysis when $R = CH_3$. In the case of $R = C_2H_5$ the hexaethyldisiloxane (yield 38%) is accompanied by a large amount of resin and by triethylphenoxysilane (24%), the latter originating from decomposition of unreacted Grignard reagent by water.

In contrast to the lower members of the series, methyl-(p-tripropylsiloxyphenyl)-carbinol is highly resistant to hydrolysis. We prepared this alcohol in 33% yield. It is a colorless liquid with a characteristic odor, boiling at $181 - 183^\circ$ (15 mm). Other reaction products were tripropylphenoxysilane (20%) formed by decomposition with water of Grignard reagent which had not reacted with aldehyde and a small quantity of resin. The absence of tripropylsilanol and hexapropylidisiloxane from the reaction products demonstrates the relatively high resistance to hydrolysis of the $Si-O-C_{ar}$ bond in the molecule of our alcohol. The molecular weight and silicon content are

$\text{ar} = \text{aromatic (carbon of the benzene ring)}.$

In good accord with the formula $(C_3H_7)_3SiOC_6H_4CH(OH)CH_3$. Hydrogen is given off when the alcohol reacts with sodium. We plotted the infrared spectrum and found an absorption band in the $3490 - 3280\text{ cm}^{-1}$ region.

The molar refraction (85.99) found for the alcohol was rather lower than the calculated value (89.21), due to the presence in our preparation of a small content of the ketone $(C_3H_7)_3SiOC_6H_4COCH_3$. The latter was formed by oxidation of the secondary alcohol group to a carbonyl group when excess of acetaldehyde is present.



The ketonic impurity was detected by the infrared spectrum which exhibited a maximum at 1684 cm^{-1} associated with conjugation of a carbonyl group with an aromatic ring ($1700 - 1680\text{ cm}^{-1}$) [3]. The experiments on synthesis of the alcohols show that the resistance to hydrolysis of $\geq Si-O-C_{ar}$ bonds increases to such an extent when propyl radicals are attached to silicon that it becomes possible to separate the corresponding alcohol.

A similar stabilizing effect of propyl radicals was not observed when attempts were made to synthesize acids of the general formula $p-R_3SiOC_6H_4COOH$. We planned to obtain the acids by decomposition of $R_3SiOC_6H_4MgBr$. Instead of the expected acids, we found in the reaction products *p*-hydroxybenzoic acid and organosilicon products of breakdown (Table 1). Formation of *p*-hydroxybenzoic acid in all cases is evidence that the above reactions took place, but the organosilicon acids were hydrolyzed with very great facility and suffered decomposition during the process of breakdown of the Grignard complexes:

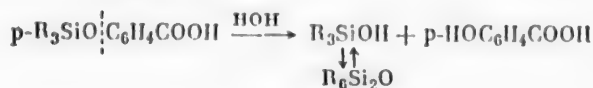


TABLE 1

Products of Decomposition of Acids $p-R_3SiOC_6H_4COOH$

R	Yield (in %)					
	R_3SiOH	R_6Si_2O	C_6H_5OH	$p-HOC_6H_4COOH$	$R_3SiOC_6H_5$	$R_3SiOC_6H_4Br$
CH_3	—	72.0	38.6	31.1	—	10.0
C_2H_5	—	68.0	36.2	26.1	—	8.4
C_3H_7	20.3	—	12.4	9.7	35.0	10.2

The instability of *p*-trialkylsiloxybenzoic acids is evidently associated with the presence of the strongly polar carboxyl group in the para-position to the trialkylsiloxy group. Judging by the yields of *p*-hydroxybenzoic acid (Table 1), the organosilicon acids were formed in yields of about 30 % in the case of $R = CH_3$ or C_2H_5 , and of about 10% when $R = C_3H_7$.

The influence of the size of the radicals attached to the silicon atom on the properties of $Si-O-C_{ar}$ bonds was experimentally established in experiments on breakdown of the Grignard reagents. The reaction goes in two steps:



The Grignard reagent is decomposed by water (when $R = CH_3$ or C_2H_5), and trialkylphenoxysilanes are formed predominantly (Table 2); hydrolysis of the latter occurs to the extent of only 20 - 22%. Decomposition with dilute hydrochloric acid (1:10) gives exclusively hexaalkyldisiloxanes when $R = CH_3$ or C_2H_5 , whereas the first reaction step predominates when $R = C_3H_7$ and tripropylphenoxysilane is only 13% hydrolyzed.

TABLE 2

Decomposition of Grignard Reagents $p\text{-R}_3\text{SiOC}_6\text{H}_4\text{MgBr}$

R	Decomposition agent	Yield (in %)				
		$\text{R}_3\text{SiOC}_6\text{H}_5$	R_3SiOH	$\text{R}_3\text{Si}_2\text{O}$	$\text{C}_6\text{H}_5\text{OH}$	$\text{R}_3\text{SiOC}_6\text{H}_4\text{Br}$
CH_3	H_2O	58.3	—	19.0	17.0	16.0
CH_3	HCl (1:10)	—	—	73.0	79.0	—
C_2H_5	H_2O	53.6	—	24.3	22.1	12.3
C_2H_5	HCl (1:10)	—	—	78.9	81.0	—
C_3H_7	HCl (1:10)	66.1	13.2	—	8.7	7.0

The greater resistance to hydrolysis of $(\text{C}_3\text{H}_7)_3\text{SiOC}_6\text{H}_5$ in comparison with the methyl and ethyl analogs must also be attributed to the screening action of the radicals at the silicon atom.

EXPERIMENTAL

Trimethyl-(*p*-bromophenoxy)-silane was obtained in 90% yield by reaction between trimethylchlorosilane and *p*-bromophenol [1] (Table 3). Triethyl- and tripropyl-(*p*-bromophenoxy)-silanes were prepared by dehydrocondensation of triethyl- and tripropylsilane respectively with *p*-bromophenol in presence of zinc chloride [2, 4] in yields of 83 and 80% (Table 3).

TABLE 3

Trialkyl-(*p*-bromophenoxy)-silanes $p\text{-R}_3\text{SiOC}_6\text{H}_4\text{Br}$

R	Boiling point (pressure in mm)	d_4^{25}	n_D^{25}	Formula	M		MR _D		% Si	
					found	calculated	found	calculated	found	calculated
CH_3	98–98.5° (7)*	1.2619**	1.5145***	$\text{C}_6\text{H}_{13}\text{OSiBr}$	—	—	—	—	11.48, 11.56	11.43
C_2H_5	141–142 (6)	1.2030	1.5170	$\text{C}_{12}\text{H}_{19}\text{OSiBr}$	285.9, 285.9	287.3	72.24	72.16	9.78, 9.85	9.75
C_3H_7	179 (13)	1.1374	1.5080	$\text{C}_{15}\text{H}_{25}\text{OSiBr}$	325.2, 326.6	329.2	86.32	86.11	8.52, 8.54	8.51

Experiments Aiming at Preparation of Methyl-(*p*-trialkylsiloxylphenyl)-carbinols

Experimental procedure. Into a round-bottomed, half-liter flask, equipped with reflux condenser, dropping funnel, and stirrer, were charged 0.17 g-atom of magnesium and 70 ml of absolute ether. After addition of 1 ml of ethyl bromide, a solution of 0.17 mole of trialkyl-(*p*-bromophenoxy)-silane in 70 ml of absolute ether was introduced gradually from the dropping funnel while the mixture was heated to the boiling point of ether. Boiling was continued for 6–8 hr. Dropwise addition was then made (with external ice water cooling) of a solution (cooled to 0°) of 0.5 mole of acetaldehyde in 70 ml of absolute ether. The mixture was boiled for 4 hr, after which decomposition was effected by stirring with 1% hydrochloric acid, ammonium chloride solution, sodium carbonate solution, or distilled water. The ethereal layer was separated, washed several times with water (100 ml each time), and dried with sodium sulfate. The ether was driven off and the products of reaction fractionally distilled.

Attempt to synthesize methyl-(*p*-trimethylsiloxylphenyl)-carbinol. The liquid separates into two layers after distillation of the ether, regardless of the agent employed for decomposition of the carbinolate (1% hydrochloric acid, water, ammonium chloride or sodium carbonate solutions). Hexamethyldisiloxane was isolated

* Literature [1]: b.p. 126° (25 mm).

** Literature [1]: d_4^{25} 1.252*** Literature [1]: n_D^{25} 1.5123

from the top layer by distillation; b.p. 99-100°, n_D^{20} 1.3773, d_4^{20} 0.7634 (see [5]). Fractional distillation of the lower layer yielded a further small quantity of hexamethyldisiloxane with b.p. 97-99° and n_D^{20} 1.3777. The resin, formed in large quantity, did not contain silicon.

Attempt to synthesize methyl-(p-triethylsiloxyphenyl)-carbinol. The carbinolate was decomposed with water. After distillation of the ether, the residue was distilled. Products of distillation were hexaethyldisiloxane with b.p. 85-86.5° (9 mm), n_D^{20} 1.4345 [5], triethylphenoxysilane with b.p. 123-128° (20 mm), n_D^{20} 1.4840 (Table 4), and unchanged triethyl-(p-bromophenoxy)-silane with b.p. 162-164° (32 mm), n_D^{20} 1.5150 (Table 3). The resin, formed in large quantity, did not contain silicon.

Synthesis of methyl-(p-tripropylsiloxyphenyl)-carbinol. Starting components were 40 g of tripropyl-(p-bromophenoxy)-silane, 3.1 g of magnesium, 16 g of acetaldehyde, and 180 ml of absolute ether. The carbinolate was decomposed with water. The following fractions were obtained after the ether had been distilled off: first 128-134° (8-10 mm), 2 g, n_D^{20} 1.4800, containing tripropylphenoxysilane; second 134-136° (8 mm), 5.6 g, n_D^{20} 1.4834, consisting of tripropylphenoxysilane (Table 4); third 146-155° (8 mm), 2.2 g, n_D^{20} 1.4960, an intermediate fraction; fourth 155-165° (8 mm), 11.3 g, n_D^{20} 1.5048. Redistillation of the last fraction gave a fraction corresponding to methyl-(p-tripropylsiloxyphenyl)-carbinol:

B.p. 181-183° (15 mm), d_4^{20} 1.0345, n_D^{20} 1.5088, MR_D 85.99; calculated 89.21.

Found %: Si 9.71, 9.65. M 292.8, 294.0, 292.0. $C_{17}H_{30}O_2Si$. Calculated %: Si 9.51. M 294.5.

Experiments with the Aim of Preparation of p-Trialkylsiloxybenzoic Acids

Grignard reagents were prepared by the procedure described above and then transferred to a flask with a large excess of pulverized solid carbon dioxide. The mixture was left to stand until it had reached room temperature and then decomposed with dilute sulfuric acid (1:15). The ethereal layer was separated and the aqueous layer extracted with a small quantity of ether. After the ethereal layer had been worked up with the calculated quantity of 2 N NaOH solution, the alkaline extracts were run into a large excess of 0.2 N hydrochloric acid solution. The precipitate, consisting in all cases of p-hydroxybenzoic acid, was purified by sublimation in vacuo (10 mm).

M.p. 209-209.5°. According to the literature [6], p-hydroxybenzoic acid has m.p. 210°. Neutralization equivalent 137.0, 137.2; calculated 138.0.

The ethereal layer was dried with sodium sulfate. The residue (after removal of the ether) was distilled to give the following fractions.

For R = CH₃: first 67-93°, n_D^{20} 1.3758, contains much hexamethyldisiloxane; second 93-100°, n_D^{20} 1.3775; after refractionation the latter had b.p. 99-100°, n_D^{20} 1.3775, d_4^{20} 0.7650 corresponding to pure hexamethyldisiloxane; third 101-176°: intermediate fraction; fourth 176-186° (crystallized in the condenser), identified as phenol (odor, blue-green color in aqueous solution with ferric chloride).

For R = C₂H₅: first 67-68° (10 mm), crystallized in condenser, identified as pure phenol; second 90-106° (10 mm), n_D^{20} 1.4530, consisting of hexaethyldisiloxane with a small admixture of phenol.

For R = C₃H₇: first 68-88° (8 mm), crystallized on standing, identified as pure phenol; second 88-89° (8 mm), n_D^{20} 1.4452, contains tripropylsilanol (see below for purification); third 89-134° (8 mm), n_D^{20} 1.4746, intermediate; fourth 134-137° (8 mm), d_4^{20} 0.9131, n_D^{20} 1.4823, identified as tripropylphenoxysilane (Table 4); fifth 168-174° (8 mm), n_D^{20} 1.5068, consisting of the original tripropyl-(p-bromophenoxy)-silane (Table 3).

The same substances were isolated on distillation when the Grignard complexes had been decomposed with water. In the case of R = CH₃ alone was a small quantity of trimethylphenoxysilane obtained [b.p. 60-63° (11 mm), n_D^{20} 1.4792 (Table 4)] apart from hexamethyldisiloxane and phenol.

Decomposition of Grignard reagents prepared from trialkyl-(p-bromophenoxy)-silanes. Grignard reagents were prepared by the above procedure. Decomposition was effected with water or dilute hydrochloric acid (1:10). The ethereal layer was dried, the ether taken off, and the residues distilled.

a) Decomposition with water. With R = CH₃, a 170-181° fraction was obtained in addition to hexamethyldisiloxane, phenol, and starting trimethyl-(p-bromophenoxy)-silane. Redistillation of that fraction yielded a substance with b.p. 65-66° (14 mm), identified as pure trimethylphenoxysilane (see Table 4 for properties). Yield

TABLE 4
Trialkylphenoxysilanes: $R_3SiOC_6H_5$

R	Boiling point (pressure in mm)		d_4^{20}	n_D^{20}	Formula	M		MR _D		% Si	
	found	according to literature	found	according to literature		found	calculated	found	calculated	found	calculated
CH ₃ [1]	65-66° (14)	81° (23)	0.9429	0.920 (d_4^{25})	C ₉ H ₁₄ OSi	159.5, 159.4	166.1	50.35	50.50	16.60, 16.49	16.80
C ₂ H ₅ [9]	111-112 (12)	243.6 (760)	0.9356	0.9293	C ₁₂ H ₂₀ OSi	206.1, 207.0	208.4	64.19	64.45	13.64, 13.58	13.46
C ₃ H ₇ [9]	145-146 (12)	275 (760)	0.9120	0.9110	C ₁₅ H ₂₆ OSi	249.0, 249.2	250.4	78.37	78.39	11.35, 11.31	11.20

58.3%. When $R = C_2H_5$, apart from small quantities of hexaethyldisiloxane, phenol, and starting substance, a 111-112° (12 mm) fraction was obtained. It was identified as triethylphenoxysilane (Table 4). Yield 53.5%.

b) Decomposition with dilute hydrochloric acid (1:10). When $R = CH_3$ or C_2H_5 , the reaction products were the corresponding hexaalkyldisiloxanes and phenol. Hexaethyldisiloxane was found in the 227-233° fraction (n_D^{20} 1.4462). Redistillations gave a fraction with b.p. 231°, n_D^{20} 1.4373. The higher refractive index was due to admixture of phenol which is difficult to remove. Distillation of the so prepared hexaethyldisiloxane with aluminum chloride gave triethylchlorosilane with b.p. 140-144°. Literature data for triethylchlorosilane [7]: b.p. 144-145° (760 mm). Two additional fractions [apart from phenol and the original tripropyl-(p-bromophenoxy)-silane] were isolated when $R = C_3H_7$. The first fraction was tripropylsilanol: b.p. 208-209°, d_4^{20} 0.8473, n_D^{20} 1.4408, MR 54.20; calculated 53.99; literature data [8]: b.p. 207°. The second fraction had b.p. 145-146° (12 mm) and was tripropylphenoxysilane (Table 4). Yield 66.1%.

SUMMARY

1. A study was made of the resistance to hydrolysis of Si-O-C_{ar} bonds in trialkyl-(p-bromophenoxy)-silanes and in the Grignard reagents and alcohols derived from the silanes.

2. It was shown that the Si-O-C_{ar} bonds of p-trialkylsiloxycarboxylic acids are not resistant to hydrolysis, and these acids undergo hydrolysis with formation of the corresponding silanols and p-hydroxybenzoic acid.

3. Three substances not previously described in the literature were prepared and characterized: triethyl- and tripropyl-(p-bromophenoxy)-silanes and methyl-(p-tripropylsiloxycarbinyl)-carbinol.

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REACTIONS OF CARBON TETRACHLORIDE WITH HOMOLOGS OF BENZENE

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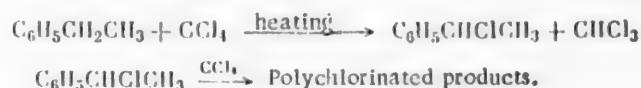
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Reactions of carbon tetrachloride with unsaturated compounds [1], which proceed in presence of initiators, have been studied fairly closely, but those of carbon tetrachloride with saturated systems have been little studied. Work has been done on reactions with aliphatic hydrocarbons [2], alcohols [3-6], aldehydes [7], etc. These reactions can be effected only at high temperature [200° and higher] or in presence of initiators (a peroxide or light). One of us [8] previously showed that carbon tetrachloride reacts with toluene at 225-235° in the absence of initiators with replacement of hydrogen by chlorine in the side chain.

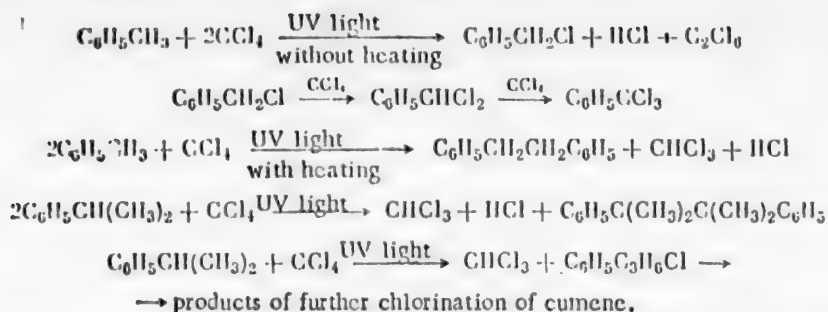
In the present work we investigated the thermal reactions of carbon tetrachloride with ethylbenzene and cumene at 220-225°, and also reactions of carbon tetrachloride with toluene and cumene at room temperature, and with toluene at 76°. The character of the reaction of carbon tetrachloride with ethylbenzene and cumene was similar to that of the reaction with toluene [8]: chlorination only took place in the side chain of ethylbenzene or cumene.* Reaction of ethylbenzene with CCl_4 gives chloroform, HCl , α -chloroethylbenzene, and polychloro derivatives of ethylbenzene. The yield of α -chloroethylbenzene was lower than that of the polychloro derivatives, and the quantity of the latter increased with increasing proportion of CCl_4 in the reaction mass. The chlorine content of the polychloro compounds was equivalent on the average to 3-4 atoms per molecule of ethylbenzene. The reaction course may be represented by the equations:



Hydrogen chloride may be formed by cleavage from the polychloro derivatives, and also by detachment of hydrogen by a chlorine atom (since $\text{CCl}_4 \rightarrow \text{Cl}^\cdot + \cdot\text{CCl}_3$). Thermal reaction with cumene similarly gave chloroform, HCl , and polychloro derivatives of cumene (the average molecular weight corresponded to trichlorocumene). Temperature and co-reagent have a marked influence on the behavior of the trichloromethyl radical. Photoreaction of CCl_4 with toluene at room temperature gave hexachloroethane, α, α, α -trichlorotoluene, $\bullet\bullet$ benzylidene chloride, $\bullet\bullet$ and HCl . When performed at the boiling point, this photoreaction yielded chloroform, benzyl chloride, and bibenzyl. Hexachloroethane was not found.

The results show that the trichloromethyl radical dimerizes only at room temperature; at higher temperatures it is converted to chloroform. In the case of cumene, whose α -hydrogen atom is easily split off, the $\cdot\text{CCl}_3$ radical detached hydrogen even at room temperature; dimerization of the $\cdot\text{CCl}_3$ radical was not observed. In the reaction products were found chloroform, HCl , bicumyl, and polychloro derivatives of cumene. The reaction course may be represented by the following equations:

- *Entry of chlorine into the aromatic ring was never observed in any of the reactions that we investigated.
- $\bullet\bullet$ Verified by hydrolysis to benzoic acid and benzaldehyde.



Bibenzyl and bicumyl are formed during photoreaction of CCl_4 with toluene by dimerization of the benzyl and cumyl radicals.

EXPERIMENTAL

Thermal reactions were carried out in thick-walled glass tubes which were filled with reaction mixture, sealed, and heated in a Carlus furnace. The tubes were afterward opened, the reaction mixture was washed with water, and the wash waters analyzed for their HCl content. After drying with CaCl_2 , the reaction products were fractionated.

Photoreactions at room temperature. The reaction mixture was poured into wide quartz test tubes which were then filled with nitrogen, closed, and irradiated by ultraviolet light from a PRK-4 lamp at a distance of 20 cm. Solid KOH was inserted in each tube as an absorbent of HCl. After completion of the reaction, the reaction mixture was washed, the wash liquors were added to the absorbent, and their chlorine content was determined by the Volhard method. The reaction mass was then fractionated.

Photoreaction while heating. Reaction was effected in a quartz flask fitted with a reflux condenser. Nitrogen was passed through the system. A PRK-4 lamp was sealed into the inside of the flask via a quartz tube; the heat of the lamp maintained the reaction mass at the boil. Hydrogen chloride was taken off into a wash-bottle (water) and determined by titration with 0.01 N NaOH. The reaction mixture was then fractionally distilled.

Thermal reaction of carbon tetrachloride with ethylbenzene. A mixture of 153.8 g of CCl_4 and 53.0 g of ethylbenzene was heated for 15 hr at 220–225°. Hydrogen chloride came off violently when the tube was opened. The reaction mixture had a dark color due to resinification. The hydrogen chloride content (net allowing for the HCl lost when the tube was opened) was 1.82 g. Fractionation of the mixture in a 25-plate column gave chloroform (b.p. 61.5, n_D^{20} 1.4466). Positive test with resorcinol. The chloroform content of the intermediate fraction was determined from the refractive index (comparison with the refractive indices of standard mixtures of CCl_4 and CHCl_3). A total of 6.7 g of chloroform was obtained.

After unreacted CCl_4 and ethylbenzene had been taken off, 2.63 g of α -chloroethylbenzene was collected [b.p. 80–85° (21 mm)]. Hydrolysis of the latter by potassium carbonate and sodium carbonate solution gave α -phenylethyl alcohol; the α -phenylethyl ester of 3,5-dinitrobenzoic acid had m.p. 94.5–95°. In addition, 6.68 g of the following fraction was obtained: b.p. 132–135° (10 mm). M 227.

Found %: C 44.25, 43.99; H 3.55, 3.53; Cl 52.9, 52.6.

Oxidation of the fraction by alkaline permanganate gave only benzoic acid with mp. 122°. A mixture with pure benzoic acid melted at the same temperature. The infrared spectrum of the fraction indicated absence of chlorine from the aromatic ring. The distillation residue was 2.43 g of resin which was not further investigated. An experiment with 127.7 g of CCl_4 and 18.0 g of ethylbenzene gave 1.45 g of HCl, 5.09 g of CHCl_3 , 1.23 g of α -chloroethylbenzene, 7.48 g of 132–135° (10 mm) fraction, and 1.13 g of resin.

Thermal reaction of carbon tetrachloride with cumene. A mixture of 127.7 g of CCl_4 and 20.4 g of cumene was heated for 15 hr at 220–225°. The reaction products were worked up as in the preceding experiment to give 1.45 g of HCl, 1.37 g of chloroform, 2.63 g of colorless oil with b.p. 127–128° (13 mm), n_D^{20} 1.5577, molecular weight 223 (chlorine content 44.65, 44.40%). Oxidation of the product with alkaline permanganate gave benzoic acid with m.p. 122°. The infrared spectrum indicated absence of chlorine from the ring. The residue was 1 g of resin.

Photoreaction of carbon tetrachloride with toluene without heating. A mixture of 346 g of CCl_4 and 104 g of toluene was irradiated for 100 hr. There was obtained 1.46 g of HCl . Distillation of unreacted CCl_4 and toluene left 2.88 g of a substance with b.p. $60-104^\circ$ (11 mm). Sublimation of a sample of this substance over concentrated H_2SO_4 gave hexachloroethane with m.p. 183° (melting point unaltered in admixture with authentic hexachloroethane). Oxidation of the product with alkaline permanganate gave benzoic acid with m.p. 122° (no depression in admixture with an authentic sample). Saponification of this substance gave 0.5 g of benzoic acid with m.p. 122° (unchanged in a mixed melting point test); benzaldehyde was also detected (silver mirror test).

Photoreaction of carbon tetrachloride with toluene when heated. A mixture of 538.4 g of CCl_4 and 161.0 g of toluene was irradiated for 66 hr. There was obtained 0.23 g of HCl . Distillation through a rectifying column gave 1.18 g of benzyl chloride with b.p. $61-70^\circ$ (14 mm). The S-benzylthiuronium picrate with m.p. 186.5° was obtained. In addition, distillation at $136-140^\circ$ (12 mm) gave 0.33 g of bibenzyl with m.p. 52° (from alcohol). The dinitro derivative of bibenzyl with m.p. 176° was prepared. Extraction of the resin with hot alcohol gave an additional 0.25 g of bibenzyl. The residue contained 0.22 g of resin.

Photoreaction of carbon tetrachloride with cumene without heating. A mixture of 384.6 g of CCl_4 and 60.0 g of cumene was irradiated for 58 hr. Reaction products were 0.7 g of HCl , 1.37 g of chloroform, and 0.58 g of chlorinated derivatives of cumene with b.p. $80-100^\circ$ (10 mm). Ligroine extraction of the resin gave 0.3 g of bicumyl with m.p. 117° . A mixture with authentic bicumyl melted at the same temperature.

SUMMARY

1. Thermal reaction of carbon tetrachloride with ethylbenzene and cumene led to formation of chloroform, hydrogen chloride, and side chain-chlorinated derivatives of the hydrocarbons. Ethylbenzene also gave α -chloroethylbenzene.
2. Photoreaction of carbon tetrachloride with toluene without heating led to formation of hexachloroethane, α, α, α -trichlorotoluene, and hydrogen chloride. Photoreaction of these compounds with heating gave chloroform, bibenzyl chloride, and hydrogen chloride. Photoreaction of carbon tetrachloride with cumene without heating gave chloroform, bicumyl, hydrogen chloride, and chlorinated derivatives of cumene.

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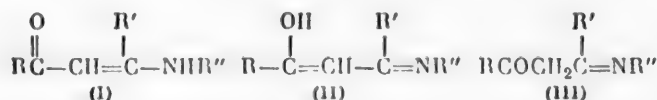
IMINES OF DI- AND POLYKETONES

IV. ULTRAVIOLET ABSORPTION SPECTRA AND STRUCTURE OF IMINES OF 2-SUBSTITUTED 1,3-INDANDIONES

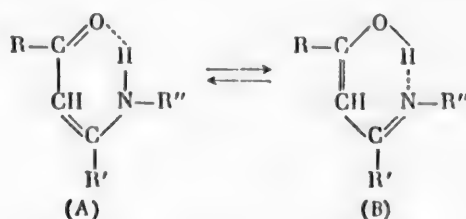
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Many β -aminovinylcarbonyl compounds—aliphatic, aromatic, alicyclic, and hemicyclic—have been described in the literature. Many methods have been devised for their preparation, and some of their properties have been described (hydrolysis, cyclization to heterocyclic compounds). Opinions differ, however, about the structure of these compounds.



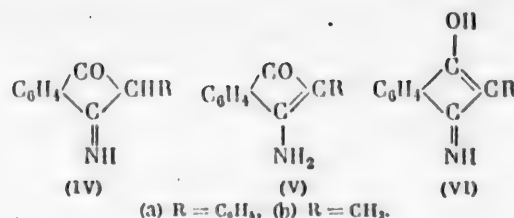
Structure (III) was rejected by Auwers and Susemihl [1] on the basis of refractometric investigations. A choice between the remaining two formulas is difficult, both being energetically favored due to conjugation and intra- or intermolecular association.



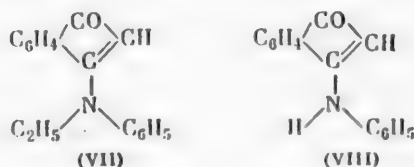
These characteristics were described by Kochetov and Dombrovskii [2]. Bonner and co-workers [3] pointed out the general impossibility of distinguishing between structures (A) and (B) on the basis of refractometric measurements. The ketoenamine structure (I) is mostly favored by authors who studied this problem with the help of ultraviolet [4-14] and infrared [4, 5, 9, 10, 15-21] absorption spectra and of Raman spectra [22].

In a previous communication [23] we described the chemical properties of the imine of phenylindandione (IV, V or VIa) and of some of its derivatives. A more detailed study was also made of the properties of the imine of methylindandione (IV, V or VIb) which will be the subject of a separate communication.

These compounds are deeply colored and do not contain carbonyl or hydroxyl groups; they also do not possess marked basic properties (see [23]). The objective of the present work was the study of the structure of imines of some 2-substituted indandiones with the help of ultraviolet absorption spectra. Starting substances were the imines of 2-methyl- and 2-phenylindandiones and the corresponding diketones. Hantzsch [24, 25] reported on the ultraviolet spectra of 2-methyl- and 2-phenylindandiones, but his data require verification. A spectroscopic study was also made of several other substances as comparison compounds.



Absorption spectra were plotted with a SF-4 spectrophotometer in the 210 – 350 m μ region. Absorption curves of methylindandione and phenylindandione and their imines are shown in Figs. 1 and 2. All these compounds have an absorption band at 215 – 225 m μ which hardly alters in position (wavelength) at different pH values. Earlier publications [24–26] also contain data for the ultraviolet spectra of indanedione derivatives, but do not report the presence of this band (the lower limit of measurements was 240 m μ). Mangini and Passerini [27] mention a 227 m μ band for indandione. Similar bands have been assigned to aromatic aldehydes and ketones (for example [28]) and to common phenyl-substituted β -aminovinyl ketones [7, 8]. The 215 – 225 m μ band accordingly corresponds to vibrations in the carbonyl group conjugated with the benzene ring. Imines of 2-substituted indandiones also possess a very strong double band at 253 – 276 m μ ($\epsilon > 3 \times 10^4$) which is the strongest for these compounds. This eliminates structure (IV) because in this region the structure (IV) would have absorbed monotonically or would have given only benzenic absorption of very much lower intensity (compare the absorption of the extremely weakly ionized phenyl- and methylindandiones, and also of indandione – at 255 m μ [27]). Consequently structures (V) or (VI) (a and b) enter into consideration for the imines. In the case of acyclic amino-vinyl ketones (see A, B) the transition from one form to the other is associated only with the overcoming of the potential barrier of the inner-molecular hydrogen bond (15.5 kcal/mole) [2]. In our case, however, such a hydrogen bond is absent, and the (V) \rightleftharpoons (VI) transition must require a very much greater energy. With the aim of solving this problem we synthesized a compound with an unequivocal enamine structure – 3-N-ethyl-N-phenylaminoindone (VII). This compound has not previously been described and was obtained by the Schlossberg method [29] from 3-bromoindone and ethylaniline. 3-Phenylaminoindone [29] (VIII) was also prepared. Comparison of the absorption spectra of 2-methylindandione imine, (VII), and (VIII) reveals the same type of absorption for all three compounds (Fig. 3).



All these compounds have a strong absorption band in the above-mentioned region (253 – 276 m μ). Attachment of a phenyl group to the nitrogen atom leads to some general changes in absorption. The 253 – 276 m μ band becomes appreciably broader, and the absorption of aniline (or of substituted aniline) becomes superposed on it. The consequence is the development of an additional band or of an inflection in the 280 m μ region and intensification of absorption in the 220 – 240 m μ region (overlapping of the B- and K-bands of aniline respectively – see for example [28]). A similar spectral additivity is reported, for example, by N. A. Valyashko [30]. It is noteworthy that the position of the 253 – 276 m μ band scarcely alters with attachment to the nitrogen atom of phenyl (VIII) or ethyl and phenyl (VII), whereas the ratio of intensities of the maxima changes appreciably (contrary to what is reported in [11]). This may possibly be due to the amino group and the ethylaniline and aniline groupings (Vb, VII, VIII) being outside the plane of the remainder of the molecule so that substitution at the amino group only results in a small hypsochromic or bathochromic shift of the absorption band characterizing this system. A similar phenomenon caused by steric hindrance is mentioned by Kiprianov [31].

In the light of the foregoing facts we are justified in assuming that the structure of the imines in a polar medium is similar to (VII), i.e. they have a ketoenamine structure and react as such. It must be noted that the above considerations are very probably applicable in particular to solutions in polar media. Kazitsyna and co-workers [32] investigated compounds of the type of salicylaldimines; the absorption spectra and interaction of groups of these compounds alter appreciably on passage from inert to polar solvents. The structure of solid imines

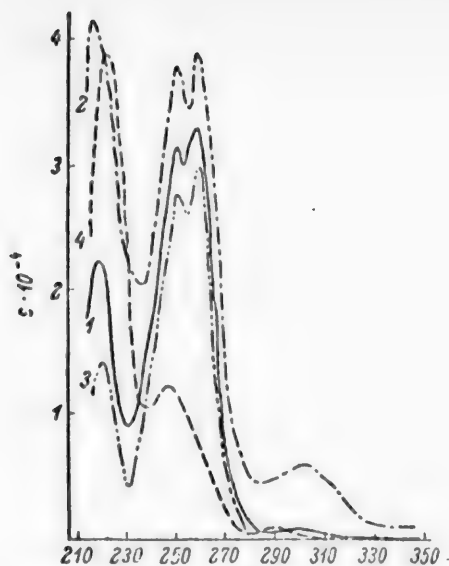


Fig. 1. Absorption curves. 1) Methylindandione imine in CH_3OH ; 2) methylindandione, with sodium methoxide, in CH_3OH ; 3) methylindandione imine, with sodium methoxide, in CH_3OH ; 4) methylindandione in CH_3OH .

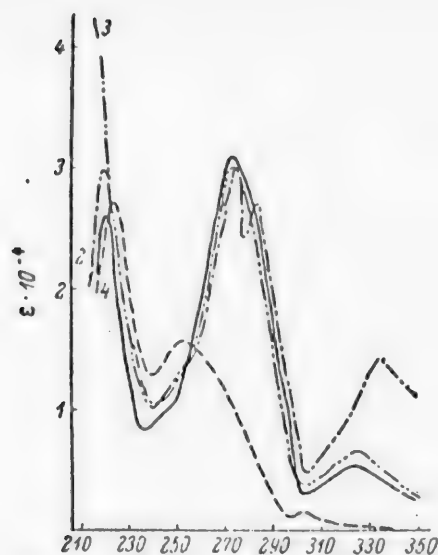


Fig. 2. Absorption curves. 1) Phenylindandione imine in CH_3OH ; 2) phenylindandione, with sodium methoxide, in CH_3OH ; 3) phenylindandione imine, with sodium methoxide, in CH_3OH ; 4) phenylindandione in CH_3OH .

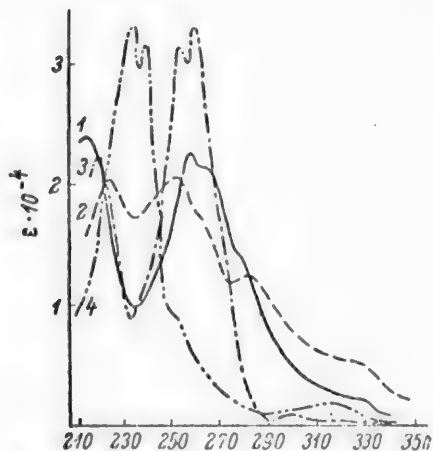


Fig. 3) Absorption curves. 1) 3-Ethylphenylaminoindone in CH_3OH ; 2) 3-phenylaminoindone in CH_3OH ; 3) methylindandione imine in CH_3OH ; 4) 3-bromoindone in CH_3OH .

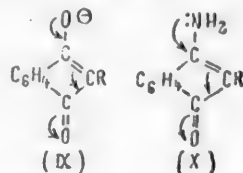
must be investigated by means of the infrared spectra, and this will be the subject of the next communication. The $253 - 276 \text{ m}\mu$ band of "imines" is a second K-band, and is excited by the vibrations in the $> \text{N} - \text{C} = \text{C} - \text{C} = \text{O}$ system. The absorption spectrum of 3-bromoindone (see table and Fig. 3) was plotted in order to demonstrate that the $253 - 276 \text{ m}\mu$ band is indeed excited by vibrations in the chromophore $\text{O} = \text{C} - \text{C} = \text{C} - \text{X}$ (where $\text{X} = \text{NH}_2, \text{NHR}, \text{NR}_2, \text{Br}$). The strong double band is shifted toward the short-wave region ($\text{X} = \text{Br}$) (relative to the nitrogen analogs of indone) as expected in view of the weaker electron-donating properties of the bromine atom [11]. Not one band but a doublet is frequently observed (see the publications of Honda [33] and Ueno [8]), but data in explanation of the phenomenon are still scanty. Finally, a third, broad absorption band has been observed at about $300 - 320 \text{ m}\mu$ in the spectra of imines and the corresponding diketones. This is probably the normal R-band of the carbonyl group. Such a band was found by Mangini and Passerini at $300 \text{ m}\mu$ in the spectrum of indandione [27]. Imines also absorb in the visible region (at about $420 - 430 \text{ m}\mu$).

Some authors [6-8, 33] observed the $300 - 350 \text{ m}\mu$ band characteristic of aminovinylcarbonyl compounds, whereas Schäd [10] found a band in the short-wave region - at $275 - 287 \text{ m}\mu$; in the case of our compounds the corresponding bands are at still longer wavelengths. We account for this difference by the impossibility in our case of formation of clathrate complexes (compare [7, 32]); in our compounds the aminovinyl ketonic grouping enters the ring with genuinely transfixed atoms and with a certain conjugation (in this connection see also [10]).

Compound	Ar-C=O		B-band		K-band		R-band	
	$\lambda_{\text{m}\mu}$	$\epsilon \cdot 10^{-1}$	$\lambda_{\text{m}\mu}$	$\epsilon \cdot 10^{-1}$	$\lambda_{\text{m}\mu}$	$\epsilon \cdot 10^{-1}$	$\lambda_{\text{m}\mu}$	$\epsilon \cdot 10^{-1}$
Phenylindandione imine	222	2.6	—	—	276	3.1	324	0.55
Ditto, in CH_3ONa	—	—	—	—	275	3.0	324	0.65
Methylindandione imine	221	2.21	—	—	254, 261	3.12, 3.27	302	0.09
Ditto, in CH_3ONa	221	1.42	—	—	253, 262	2.75, 2.97	316	(0.03)
3-Phenyl-aminoindane	225	2.06	283	1.21	253	2.03	326	0.53
3-Phenylethyl-aminoindone	216	2.39	280	1.4	258	2.25	331	0.22
3-Bromoindone	—	—	251	0.9	235, 241	3.3, 3.15	320	0.2
Phenylindandione	225	2.7	255	1.5	—	—	302	0.15
Ditto, in CH_3ONa	222	3.0	—	—	278, 285	3.0, 2.7	—	—
Methylindandione	224	3.89	248	1.2	—	—	290	(0.07)
Ditto, in CH_3ONa	218	4.11	—	—	253, 262	3.77, 3.88	—	—

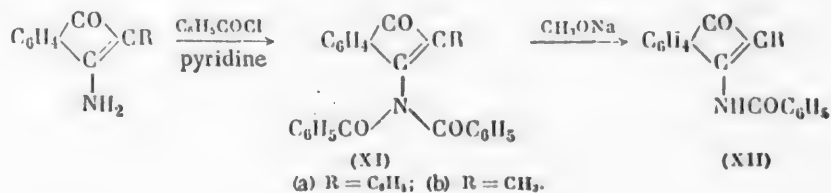
The ketoenamines (V) must be very weak acids; this implies that the 253–276 m μ bands in particular should not change appreciably after alkali treatment; the only change is in the ratio of intensities of the maxima at 220 and 270 m μ . This is also true in our case (see figures and table). Other authors have reported this phenomenon [33].

Examination of the absorption spectra of compounds of the indandione series reveals yet another interesting fact. The absorption curves of the imines closely resemble those of the corresponding diketones in an alkaline medium both in intensity and in the position of the bands. In an alkaline medium indandiones probably form the anion (IX) with uniformly distributed electron density. Such a more or less complete uniformity is also possible with aminovinyl ketones, as already noted [34]. In our case this form is represented by structure (X).

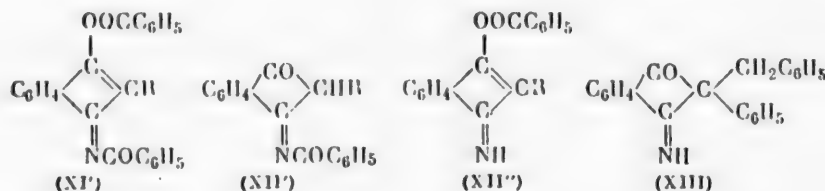


We can now understand the difficulty of proving the presence of amino and carbonyl functions in imines. We can also understand why they have a deep color and high melting point (relative to the original diketones—see Experimental and [23]), as well as why they are poorly soluble in nonpolar and weakly polar solvents (benzene, carbon tetrachloride, ether). The displacement of the unshared electron pair of the nitrogen along the chain of conjugated double bonds is reduced, for example in N-benzoyl derivatives of imines (XII), but their acidity increases appreciably; due to the amidic hydrogen, compounds (XII, a, b) are soluble in aqueous alkalis.

Compounds (XII) were prepared by the scheme:



Benzoyl derivatives (XI) and (XII) can also have other structures, for example (XI'), (XII'), (XII''), but structures (XI) and (XII) were confirmed for the benzoates by the infrared spectra (details in a forthcoming communication).



If, for example, the conjugation between the carbonyl group and the nitrogen atom is suppressed, as in compound (XIII), then the basic character of the nitrogen comes into play; (XIII) forms salts.

We take the opportunity of expressing thanks to A. Grinval'd and O. Neiland for plotting the absorption spectra.

EXPERIMENTAL

Imine of 2-methyl-1,3-indandione. The compound was prepared for the first time by student M. Kapar, but we slightly modified the procedure. To a solution of 15 g of 2-methylindandione [35] in 50 ml of glacial acetic acid was gradually added 70 g of ammonium acetate (the latter must be as dry as possible). The heated mixture became dark-red and quickly deposited red needles. After the mixture had set, it was cooled and after a day it was stirred in a liter of water, filtered, washed with water, and dried. Yield 12 g (80%). M.p. 220–221° (from water); sinters at 213°.

Found %: N 8.38. C₁₀H₈ON. Calculated %: N 8.81.

3-N-Ethyl-N-phenylaminoindone-1 (VII). To a solution of 1 g of bromoindone [29] in 5 ml of absolute alcohol was added 1.2 g of ethylaniline. The mixture was brought to the boil and then cooled; after addition of 30 ml of absolute alcohol, the mixture was allowed to stand in the cold for 2 hr. The ethylaniline hydrobromide (0.84 g) was then filtered off. The filtrate was boiled in presence of active carbon, filtered, and evaporated to dryness. The residue was dissolved in a few milliliters of benzene and ligroine was gradually added. The mixture was allowed to stand in the cold for 24 hr, filtered, washed with ligroine, and dried. Yield 0.715 g (60%). M.p. 109.5° (from a mixture of benzene and ligroine).

Found %: N 5.48. C₁₇H₁₅ON. Calculated %: N 5.62.

The substance is readily soluble in common organic solvents. It is easily cleaved by acids to form indandione and N-ethylaniline.

N,N-Dibenzoate of phenylindandione imine (XI, R = C₆H₅). A mixture of 5 g of phenylindandione imine [23], 50 ml of anhydrous pyridine, and 15 g of benzoyl chloride was boiled for 10 min. After cooling, 100 ml of ethanol and 10 ml of water were added. The next day the product was filtered, and the crystals were washed with alcohol and dried. Yield 7.4 g (76%); a yellow substance; m.p. 207–208.5° after recrystallization from glacial acetic acid.

Found %: N 3.55, 3.51. C₂₉H₁₉O₃N. Calculated %: N 3.26.

Lower yields were obtained if ordinary pyridine was used instead of the anhydrous substance. The filtrate from the dibenzoate deposited the N-monobenzoate of phenylindandione imine when poured into water.

N-Monobenzoate of phenylindandione imine (XII, R = C₆H₅). The dibenzoate of phenylindandione imine (0.5 g) in alcohol (10 ml) was boiled with excess of sodium ethoxide for 20 min. The solution became carmine. After cooling, a little water was added to dissolve the precipitated sodium salt of the N-monobenzoate of the imine and the liquid was neutralized with hydrochloric acid. Filtration was performed after an hour. Recrystallization from dilute alcohol gave orange needles; yield 0.22 g (68.5 %). M.p. 183–184° after recrystallization from acetic acid and dilute alcohol.

Found %: N 4.57. C₂₂H₁₆O₂N. Calculated %: N 4.35.

The compound is readily soluble in common organic solvents. It dissolves in concentrated aqueous caustic alkali and alcoholic alkali with a carmine color. Boiling of an alcoholic solution of the mono- and dibenzoates of the imine with hydrochloric acid results in hydrolysis to phenylindandione.

N,N-Dibenzoate of 2-methylindandione imine (XI, R = CH₃). A mixture of 2 g of methylindandione imine, 10 ml of pyridine, and 4.4 g of benzoyl chloride was boiled for 10 min. After cooling, 15 ml of alcohol and 5 ml of water were added. The following day the orange-yellow crystals were filtered and washed with alcohol. Yield 1.18 g (25.5%). M.p. 214–215° (from glacial acetic acid).

Found %: N 3.93. C₂₄H₁₇O₃N. Calculated %: N 3.81.

The filtrate after separation of the dibenzoate was poured into water. Fine crystals of the N-monobenzoate of methylindandione imine came down. Yield 1.94 g (58.7%). Orange needles; m.p. 165° (from alcohol).

Found %: N 5.55. C₁₇H₁₃O₂N. Calculated %: N 5.32.

N-Monobenzoate of methylindandione imine was also obtained by cleavage of the dibenzoate of methylindandione imine (same procedure as in the preceding experiment). The chemical properties of the mono- and dibenzoates of methylindandione imine are similar to those of the analogous derivatives of phenylindandione imine.

2-Phenyl-2-benzylindandione imine hydrochloride. To a solution of 5 g of phenylindandione imine in 13.5 ml of 3% sodium ethoxide solution and 35 ml of alcohol was added 6.7 g of benzyl bromide. The mixture was boiled for 5–10 min and cooled slightly. Addition was then made of 7 ml of concentrated hydrochloric acid. The still warm solution was filtered from sodium chloride and bromide. 2-Phenyl-2-benzyl-1,3-indandione imine hydrochloride came down from the filtrate and was filtered and washed with alcohol. Yield 4.5 g. Pale-yellow crystals with m.p. 236–237° after four recrystallizations from glacial acetic acid.

Found %: N 3.51. C₂₂H₁₅ONCl. Calculated %: N 4.03.

The salt is slightly soluble in water but hydrolyzes when heated (see below). The chlorine is in ionogenic combination (precipitate with silver nitrate).

Hydrolysis of 2-phenyl-2-benzylindandione imine hydrochloride. The salt (0.5 g) was boiled in alcohol (10 ml) with concentrated hydrochloric acid (5 ml) for an hour. White needles came down on cooling; m.p. 103°; no depression in admixture with authentic 2-phenyl-2-benzylindandione [36]. The ammonium was detected in solution.

2-Phenyl-2-benzylindandione imine (XIII). 2-Phenyl-2-benzylindandione imine hydrochloride was treated in the cold with 3% sodium ethoxide. The solution was diluted with water, and the precipitate was filtered and twice recrystallized from alcohol. White crystals (m.p. 101.5–102.5°), soluble in common organic solvents.

Found %: N 4.64. C₂₂H₁₇ON. Calculated %: N 4.50.

When treated in the cold with concentrated hydrochloric acid, an alcoholic solution of the substance gives the imine salt (see above). 2-Phenyl-2-benzylindandione imine is hydrolyzed to 2-phenyl-2-benzylindandione with very great facility when heated with acids.

SUMMARY

Ultraviolet absorption spectra of some 2-substituted indandiones and of the products of their reaction with ammonium acetate (so-called imines) were plotted. The imines probably have an enamine structure in alcoholic solution. Some of the physical and chemical properties of the imines and of their alkyl and acyl derivatives are explained in the light of the proposed structure of the imines.

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IMINES OF DI- AND POLYKETONES

V. INFRARED ABSORPTION SPECTRA AND STRUCTURES OF IMINES OF 2-SUBSTITUTED INDANDIONES AND SOME OF THEIR DERIVATIVES

Ya. F. Freimanis and G. Ya. Vanag

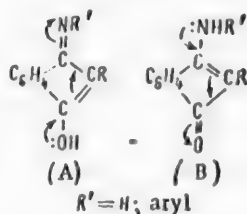
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There has been very little work on infrared spectroscopy of indan derivatives, and the absorption of the compounds studied is usually given in the form of isolated bands [1-5]. In a previous communication [6] data were published on the ultraviolet spectroscopy of imines of 2-substituted indandiones. Since for compounds with possible prototropic conversions the ultraviolet absorption spectra can indicate their actual structure only in solution, we are concerned in the present work with the structure of these imines in the solid phase. For this purpose, infrared absorption spectra of the imines were measured in an immersion medium (vaseline oil) and in solution. In addition, spectra were measured for comparison on a number of other compounds. For the imines of 2-substituted indandiones, two formulas are under consideration: the iminoenol (A) and the ketoenamine (B) (compare [6]).



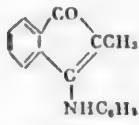
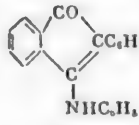
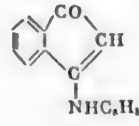
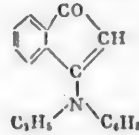
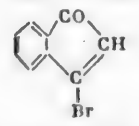
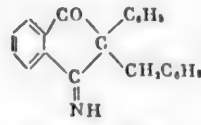
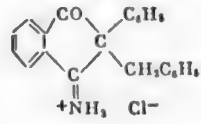
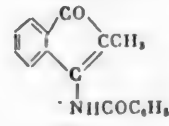
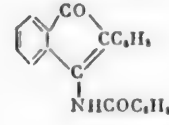
The substances investigated and their absorption are listed in Tables 1 and 2.

3 μ Region. The available literature data in this frequency region for aminovinylcarbonyl compounds are rather contradictory. Even in the case of derivatives of β -aminocrotonic ester, where only the valence vibrations of the N-H group may be considered, frequencies from 3100 to 3340 cm^{-1} are observed, which are attributed to the vibrations of free or associated N-H groups [7-9]. In the case of β -aminovinylketones, where equilibrium may exist between the ketoenamine and the iminoenol, the possibilities of vibrations are still greater, and their study is still more complex [10-14]. On the question of which frequencies pertain to valence vibrations of the N-H group and which to the O-H group, there are no reasonably valid observations except those given in an article by Weinstein and Wyman [14]. This work represents the first systematic study in attacking the problem of the structure of β -aminovinylketones.

Since it is easier to distinguish the absorption bands of phenylaminoindones (III) - (V), the discussion will be started with these compounds. The phenylaminoindones (III) and (IV) have two absorption bands at about 3190-3375 cm^{-1} , and Compound (V) has one at 3182 cm^{-1} . Since in dichloroethane solution the lower frequency disappears but the higher frequency remains [for (V) the higher frequency makes its appearance], it is obvious that the frequencies near 3375 cm^{-1} correspond to the free valence vibrations of the N-H group, and the frequencies

TABLE 1

Substances for which Infrared Spectra were Measured*

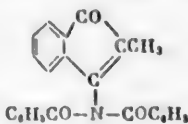
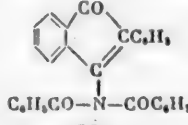
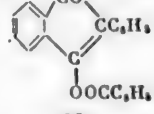
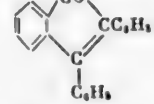
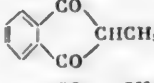
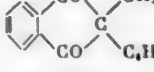
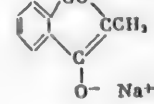
Formula no.	Name of compound	Formula	Medium
(I)	Imine of methylindandione	(A) or (B); $R=CH_3$	VO (Ia) ^{••} D (Ib) ^{•••}
(II)	Imine of phenylindandione	(A) or (B); $R=C_6H_5$	VO (IIa) D (IIb)
(III)	2-Methyl-3-phenylaminoindone		VO (IIIa) D (IIIb)
(IV)	2-Phenyl-3-phenylaminoindone		VO (IVa) D (IVb)
(V)	3-Phenylaminoindone		VO (Va) D (Vb)
(VI)	3-N-Ethyl-N-phenylaminoindone		VO (VIa) D (VIb)
(VII)	3-Bromoindone		VO
(VIII)	1-Keto-2-phenyl-2-benzyl-3-iminoindan		VO
(IX)	Hydrochloride of (VIII)		VO
(X)	2-Methyl-3-benzamidoindone		VO
(XI)	2-Phenyl-3-benzamidoindone		VO

* Absorption spectra were measured by an IKS-12 spectrophotometer with NaCl prism.

•• VO = vaseline oil.

••• D = 1,2-dichloroethane.

TABLE 1 (continued)

Formula no.	Name of compound	Formula	Medium
(XII)	2-Methyl-3-N,N-dibenzoyl-aminoindone		VO
(XIII)	2-Phenyl-3-N,N-dibenzoyl-aminoindone		VO
(XIV)	2-Phenyl-3-benzoyloxyindone		VO
(XV)	2,3-Diphenylindone		VO
(XVI)	2-Methylindandione		VO
(XVII)	2-Methyl-2-phenyl-indandione		VO
(XVIII)	Sodium salt of 2-methyl-indandione		VO

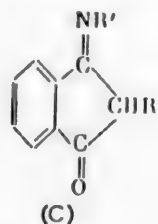
at 3190 cm^{-1} to the valence vibrations of the associated N-H group (here and elsewhere the question is one of intermolecular association). Similar valence vibration frequencies of N-H groups are also found for the imine benzoates (X) and (XI), at 3181 and 3175 cm^{-1} respectively.

For β -acetamidocrotonic ester a frequency of 3225 cm^{-1} is cited [15], and for acylated vinylamines 3450 cm^{-1} [16]. The fact that we are here dealing with just the vibrations of N-H groups will be obvious from the following. The free imines (I) and (II) in solution also show vibrations at 3360 - 3380 cm^{-1} . In addition, a 3396 cm^{-1} frequency is found for (II) in the solid form; apparently the imine of phenylindandione has less complete intermolecular bonding, so that the frequency of free vibrations of the N-H group also appears. In the solid form (I) and (II) have two groups of bands, at 3070 and 3283 cm^{-1} for (I) and at 3108 and 3262 cm^{-1} for (II). These probably represent valence vibrations of bonded OH and NH groups; it is assumed that just the larger values of ν correspond to the vibrations of the N-H group. There are some grounds for this assumption (see further). In solution, (I) and (II) show the previously mentioned frequencies near 3370 cm^{-1} , which correspond to free vibrations of N-H groups, and frequencies near 3470 cm^{-1} , which correspond to free or weakly bonded vibrations of OH groups.

6 μ Region. In the double-bond region a number of frequencies have been observed by several authors [10-13]. The highest frequency, about 1600 cm^{-1} , is usually ascribed to valence vibrations of $>\text{C}=\text{O}$ [10-12]. In their opinion the lower frequencies represent $\text{C}=\text{C}$ and $\text{C}=\text{N}$ double bonds, deformation vibrations of N-H groups, and others. In their article Dombrovskaya and co-authors [13] assume that the frequency $\nu_{\text{C}=\text{O}}$ occurs below the frequency $\nu_{\text{C}=\text{C}}$. It is hardly possible to agree with this, as such a location of the bands contradicts all available experience [17]. Since the authors [10-13] investigated β -aminovinylketones only in the solid phase or melt (substances were studied in solution only in isolated cases [13]), it is necessary to exercise caution in agreeing

with the proposed correspondence of frequencies to any definite group. Recently Weinstein and Wyman [14] investigated β -aminovinylketones in solution and thereby avoided the effect of hydrogen bonds on the frequencies of the groups determined. They proved conclusively the existence of $>\text{C}=\text{O}$ and NH_2 groups in the compounds and clearly distinguished the absorption bands corresponding to these groups.

The results which we obtained show once again that not one of the nitrogen-containing compounds which we described [except (VIII) and (IX)] exists in the ketimine form (C). Compound (VIII) served as a model. Here there are valence vibration frequencies of $>\text{C}=\text{O}$ and $\text{C}=\text{N}$ groups at 1715 and 1649 cm^{-1} respectively. In the remaining compounds the two frequencies are not present together. We had already demonstrated this earlier [6].



Diketo compounds have valence vibration frequencies of $>\text{C}=\text{O}$ groups in the order of 1710 and 1745 cm^{-1} [for (XVI) at 1706 and 1743 cm^{-1} , and for (XVII) at 1710 and 1747 cm^{-1}].

First let us review the spectra of Compounds (III)-(VI). In the solid form all of them have bands near 1660 - 1670 cm^{-1} which we attribute to valence vibrations of the $>\text{C}=\text{O}$ group [in accord with Formula (B)]. In solution this frequency is shifted for (III)-(V) on the average 20 cm^{-1} in the direction of higher values of ν . This frequency for (VI) also undergoes a slight shift. From this it may be concluded that in the solid form the phenylaminoidones (III)-(V) [Formula (B), $\text{R}' = \text{C}_6\text{H}_5$] are partially associated and have a strong intermolecular hydrogen bond of the type $\text{N}-\text{H} \dots \text{O}=\text{C}$; in addition, the molecules probably affect each other also as dipoles [shift of (VI)]. In the solid form Compounds (III) and (IV) have two more frequencies, in the regions 1593 - 1601 and 1565 - 1585 cm^{-1} . The first band is caused by deformation vibrations of the bonded N-H group; this frequency is not observed in solution. The free deformation vibrations of the N-H group correspond to the 1565 - 1585 cm^{-1} frequency. For (III) and (IV) the association is partial, since in the solid form they have both of these bands, and in addition have a band of free valence vibrations of the N-H group (see Table 2). Compound (V) is associated completely;

TABLE 2
Absorption of Substances Studied *

(Ia)	(Ib)	(IIa)	(IIb)	(IIIa)	(IIIb)	(IVa)	(IVb)	(Va)	(Vb)	(VIa)	(VIb)	Origin
$\frac{1546}{73}$	—	$\frac{1546}{62}$	—	$\frac{1544}{85}$	$\frac{1527}{20}$	$\frac{1534}{86}$	$\frac{1528}{23}$	$\frac{1539}{94}$	$\frac{1556}{48}$	$\frac{1554}{79}$	$\frac{1550}{70}$	$\nu_{\text{C}=\text{C}}$
$\frac{1574}{48}$	$\frac{1585}{41}$	$\frac{1574}{23}$	$\frac{1571}{29}$	$\frac{1577}{79}$	$\frac{1585}{43}$	$\frac{1564}{78}$	$\frac{1575}{45}$	—	$\frac{1565}{50}$	—	—	Free δ_{NH}
—	—	—	—	$\frac{1601}{65}$	—	$\frac{1595}{53}$	—	$\frac{1596}{73}$	—	—	—	Bonded δ_{NH}
$\frac{1613}{41}$	$\frac{1611}{39}$	$\frac{1611}{40}$	$\frac{1603}{28}$	$\frac{1617}{59}$	$\frac{1619}{27}$	$\frac{1610}{45}$	$\frac{1611}{25}$	$\frac{1609}{44}$	$\frac{1602}{26}$	$\frac{1598}{40}$	$\frac{1600}{15}$	$\nu_{\text{C}=\text{C}}$ in benzene ring
$\frac{1637}{60}$	$\frac{1638}{63}$	$\frac{1634}{59}$	$\frac{1634}{52}$	—	—	—	—	—	—	—	—	$\nu_{\text{C}=\text{N}}$

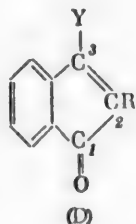
* Absorption of the substances is presented in the form of fractions: The frequencies of the maxima are given in the numerator, and their intensity in the particular experiment is given in the denominator. The frequencies of the valence and deformation vibrations of CH_3 -, $-\text{CH}_2$ -, and $>\text{CH}$ groups are not presented, since the medium for the measurements was vaseline oil or dichloroethane. Compounds (I)-(VI) have low solubility in carbon tetrachloride.

TABLE 2 (continued)

(Ia)	(Ib)	(IIa)	(IIb)	(IIIa)	(IIIb)	(IVa)	(IVb)	(Va)	(Vb)	(VIa)	(VIb)	Origin
1685 24	1689 34	—	1687 20	1664 58	1681 26	1662 61	1682 21	1660 65	1683 22	1669 65	1673 30	$\nu_{C=O}$
—	—	—	—	—	1741 18	—	—	—	1729 19	—	—	?
3070 59	—	3108 37	—	—	—	—	—	—	—	—	—	Bonded ν_{OH}
3283 44	—	3262 22	—	3191 52	—	3191 52	—	3182 56	—	—	—	Bonded ν_{NH}
—	3376 22	3396 21	3367 17	3371 51	3365 11	3379 36	3341 4	—	3388 10	—	—	Free ν_{NH}
—	3470 21	—	3469 15	—	—	—	—	—	—	—	—	Free ν_{OH}
(VII)	(VIII)	(IX)	(X)	(XI)	(XII)	(XIII)	(XIV)	(XV)	(XVI)	(XVII)	(XVIII)	Origin
—	1590 49	—	1508 61	1519 86	—	—	—	—	—	—	—	Bonded δ_{NH}
—	—	—	—	—	—	1585 41	1593 58	—	—	1502 56	—	$\nu_{C=C}$ in benzene ring
1599 56	1599 57	1593 69	1601 57	1602 53	1602 50	1600 51	1600 59	1600 42	1594 66	1596 68	1619 46	$\nu_{C=C}$ in benzene ring
1541 69	—	—	1583 52	1585 52	1624 39	1623 36	1638 55	1610 43	—	—	1510 97	$\nu_{C=C}$
—	1649 73	—	—	—	—	—	—	—	—	—	—	$\nu_{C=N}$
—	—	—	1641 84	1656 89	1673 80	1691 90	—	—	—	—	—	Amide $\nu_{C=O}$
1720 89	1715 88	1707 79	1706 68	1706 72	1704 75	1703 91	1717 87	1704 91	1706 85	1710 91	1566 73	$\nu_{C=O}$ of ring
—	—	1744 75	1735 28	1717 65	—	—	—	—	1743 70	1747 58	—	$\nu_{C=O}$ of ring
—	—	—	1652 82	—	1719 67	1715 77	—	—	—	—	—	Amide $\nu_{C=O}$
—	—	—	—	—	—	1772 19	—	—	—	—	—	Amide $\nu_{C=O}$
—	—	—	—	—	—	—	1740 91	—	—	—	—	Ester $\nu_{C=O}$
—	—	1684 91	—	—	—	—	—	—	—	—	—	$\nu_{C=N^+}$
—	3191 62	3386 48	3181 61	3175 67	—	—	—	—	—	—	—	ν_{NH}

In the solid phase the $1565\text{--}1585\text{ cm}^{-1}$ frequency does not exist, nor does the free valence vibration frequency of the N-H group. Compounds (III)–(VI) have a frequency at $1598\text{--}1619\text{ cm}^{-1}$, which is little changed in solution. This represents the vibration frequencies of the double bonds in the benzene ring. In the present case the phenomenon described by Weinstein and Wyman [14] is observed: In solution the bands of the δ_{NH} and $\nu_{\text{C=O}}$ frequencies are shifted in opposite direction.

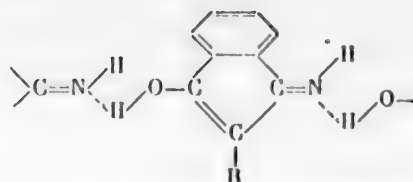
The position of the valence vibration bands of the >C=O group is also characteristic. The indan system, possessing a five-membered ring, in general shows small shifts of the valence vibration frequency of the >C=O group either upon conjugation or upon introduction of a nucleophilic substituent into the five-membered ring. In cyclopentanone systems introducing a double bond into the α, β position (relative to the carbonyl group) gives rise to the normal displacement of valence vibration frequencies of the >C=O group (for example, [18–19]); on the contrary, in the pair indanone–indone an increase of frequencies is observed upon introducing a double bond into the five-membered ring. For indanone $\nu_{\text{C=O}}$ occurs at 1698 cm^{-1} [5] in the solid phase and at 1708 cm^{-1} in solution [2]; for 4,7-dimethoxyindanone in solution, 1703 cm^{-1} [2]. For 2,3-dimethylindone this frequency occurs at 1700 cm^{-1} (in the solid form) or 1712 cm^{-1} (in carbon disulfide) [4]; according to our data for 2,3-diphenylindone, $\nu_{\text{C=O}}$ occurs at 1704 cm^{-1} (in solid form). For this substance Josien cites frequency values of 1698 cm^{-1} (in solid form) or 1713 cm^{-1} (in carbon disulfide) [4]. Further, it would be expected that upon introducing a nucleophilic group (Y) into position 3 [see (D)], the shift of $\nu_{\text{C=O}}$ in the direction of lower frequencies will be relatively small. As is evident from the data of Table 2, this is actually true (shift $\sim 20\text{ cm}^{-1}$). Possibly this phenomenon is connected with strain in the five-membered ring. At the same time, a shift of $\nu_{\text{C=O}}$ up to 80 cm^{-1} is observed for acyclic compounds (see for example [17]).



For the imines (I) and (II) a band at $1634\text{--}1638\text{ cm}^{-1}$ is observed both in the solid form and in solution. This indicates either that the bond in question does not participate in hydrogen bond formation (compare the 3μ region), or that there are only nonplanar hydrogen bonds which have little effect on the valence vibration frequencies of the double bonds [20]. Fabian and co-workers indicate that the frequency $\nu_{\text{C=N}}$ in general is little changed either upon association or upon conjugation [21]. We attribute the $1634\text{--}1638\text{ cm}^{-1}$ frequency to valence vibrations of the C=N group, since this frequency is too low for the >C=O group. Fabian and co-workers indicate a fairly wide range ($1610\text{--}1670\text{ cm}^{-1}$) for the frequency of the C=N group [21,22]. Pickard and Polly give a somewhat sharper frequency range, $1605\text{--}1655\text{ cm}^{-1}$ [23]. Opportunely, the frequency of an unconjugated C=N group in the indan system occurs at 1649 cm^{-1} [Compound (VIII)]; therefore, for Compounds (I) and (II), in accord with Formula (A), the frequency of valence vibrations of the C=N group should be expected in exactly the range of frequencies which is observed. Hence, in the imines (I) and (II) in the solid phase the iminoenol form predominates. The deformation vibration frequencies of the N-H group are little changed upon transition from the solid substance to a solution. This signifies that the imine hydrogen atom takes little part in hydrogen bonding (compare the frequency of 3396 cm^{-1} for (II) in the solid form). This case confirms the assumption on the origin of the bands in the $3250\text{--}3300\text{ cm}^{-1}$ region for Compounds (I) and (II) (see above).

Another case is of interest. For (I) in the solid form a weak band appears at 1685 cm^{-1} . This same band appears for Compounds (I) and (II) in solution. From the foregoing it follows that this is the vibration frequency of the nonassociated carbonyl group. Hence in nonpolar solvent also, a certain portion of the imines (I) and (II) is converted from form (A) to form (B). This demonstrates the possibility of rather ready conversion of the tautomeric forms $A \rightleftharpoons B$ even in the absence of intramolecular hydrogen bonding (compare [6]). As was shown previously [6], in methanol medium it is considered that the ketoenamine form predominates.

In this connection we propose that in the solid form the imines (I) and (II) exist in the form of chain "polymers".

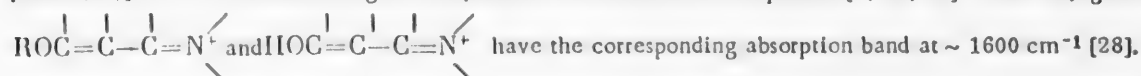


The imine (I) evidently contains also a small quantity of the enamine (B) in the solid form. From the low values of the valence vibration frequency of the OH groups, it follows that the hydrogen atom in the hydroxyl group is rather loosely bound (compare [24]). Upon dissolving, depending upon the polarity of the solvent, either free molecules of the ketoenamine (B) (in methanol) or the iminoenol (A) (in dichloroethane) may be formed preferentially. O'Sullivan and Sadler also point out a similar coupling of molecules into chain polymers in the case of 3-formylindole. They also assume a similar breaking of the bonds upon dissolving the substance [25].

Compounds (I) - (VI) in the solid form have a very intense absorption band at 1530-1555 cm^{-1} . A similar band is also observed by other authors [10-13]; they attribute this band to vibrations of the polarized double bond $\text{C}=\text{C}$ (in β -aminovinylketones this has to some extent a "sesqui-" character). Mecke and Funck [29] also point out a similar phenomenon for acetylacetone. In our opinion the 1530-1555 cm^{-1} frequencies for Compounds (I)-(VI) should be attributed expressly to vibrations of the double bond in the five-membered ring. A similar band is also shown by 3-bromoindone (VII) (at 1541 cm^{-1}).

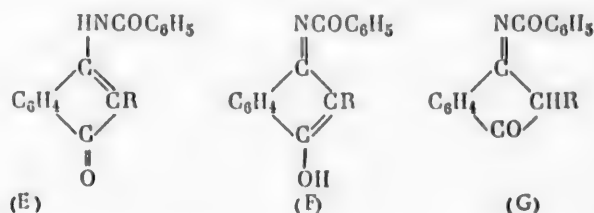
The sodium salt of methylindandione has an absorption band at 1510 cm^{-1} . The band at 1520-1555 cm^{-1} for 3-phenylaminoindones (III)-(VI) is decreased in intensity upon dissolving the substance, and for (I) and (II) it disappears completely; possibly it is shifted in the direction of lower frequencies and is masked by the background absorption. This phenomenon cannot be explained at present. The appearance of certain secondary bands is also unexplained; for example, Compounds (III) and (V) show a slight absorption above 1700 cm^{-1} .

The unconjugated $\text{C}=\text{NH}_2^+$ group of derivatives of 2,2-disubstituted indandiones absorbs at 1684 cm^{-1} [Compound (IX)], i.e., in the usual range of frequencies for ammonium compounds [9, 26, 27]. The conjugated systems



The N-benzoyl derivatives of imines of methyl- and phenylindandiones occupy a rather special position. They were obtained as substances for comparison in the previous phase of the studies [6]; it was necessary to establish their structure firmly.

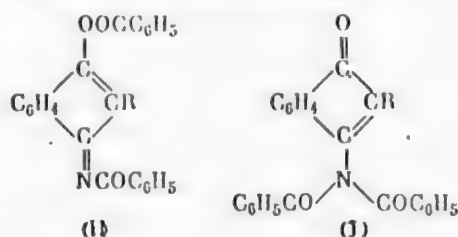
The N-monobenzoates of imines (X) and (XI), judging by their chemical properties, could have the following structures.



The form (G) is eliminated, since it should not absorb in the 3μ region and should absorb near 1630 cm^{-1} (vibration frequency of the $\text{C}=\text{N}$ group in acylimines [30]), which was not observed. As already indicated above, a frequency appears in the 3180 cm^{-1} region (vibrations of associated N-H groups). Compounds (X) and (XI) absorb in the 1650 cm^{-1} region (absorption of the amide carbonyl [16,17]), and in two bands above 1700 cm^{-1} . This undoubtedly indicates the structure (E). The band near 1510 cm^{-1} possibly corresponds to deformation vibrations of the N-H group, since in the dibenzoates (XII) and (XIII) this frequency is absent. Rosenkranz cites a 1520 cm^{-1} frequency for acylenamines [16]. The band near 1585 cm^{-1} is attributed to vibrations of the polarized double bond in the five-membered ring. We will deal later with the question of why two valence vibration frequencies appear for the $\text{C}=\text{O}$ group, and two amide frequencies for (X).

2-Phenyl-3-benzoyloxyindone (XIV) has absorption entirely as expected: frequency of the benzoate carbonyl at 1740 cm^{-1} (compare $\nu_{\text{C}=\text{O}}$ of vinyl esters [17,31]), frequency of the ring carbonyl group at 1717 cm^{-1} , frequency of the double bond at 1638 cm^{-1} , and strong benzene absorption at 1593 and 1600 cm^{-1} .

The dibenzoates of imines of methyl- and phenylindandione (XII) and (XIII) may be assigned the structures (II) or (I), in accordance with their chemical behavior (see [6]).



The structure (II) is improbable, as the benzoate carbonyl frequency is not observed, and the appearance of bands near 1700 cm^{-1} is not explainable. The structure (I) remains as the most probable. The frequency near 1703 cm^{-1} corresponds to the valence vibrations of the ring carbonyl group, since Compounds (XII) and (XIII) should absorb similarly to free indenes. In addition, there are a number of bands in the range $1670\text{--}1770\text{ cm}^{-1}$. They are attributed to vibrations of the amide carbonyl groups. Actually, the dibenzoates (XII) and (XIII) are symmetrically constructed systems conforming to (I); here splitting of the carbonyl bands into two or even three bands is expected. This phenomenon was also observed by Abramovitch [32]. A similar splitting of frequencies of the $\text{C}=\text{O}$ groups is also observed for the monobenzoates (X) and (XI), since they may be considered as vinylogs of diacylamines. Other authors [19, 33, 34] also point out splitting of carbonyl bands. The band near 1625 cm^{-1} corresponds to vibrations of the double bond of the five-membered ring, and the remaining frequencies to benzene absorption. As is evident from the results, the band of the $\text{C}=\text{C}$ double bond undergoes displacement in the direction of higher frequencies upon weakening of the electron-donor properties of the nitrogen atom in the series: (a) unsubstituted or N-arylketoenamine, (b) N-acylketoenamine, (c) N-diacylketoenamine.

From the structure (I), the easy cleavage of (XII) and (XIII) to (X) and (XI) respectively may be understood (see [6]). Such a phenomenon was also observed by Davidson and Skovronek [35].

EXPERIMENTAL

Method of Measuring Spectra. The spectra were measured with an IKS-12 spectrophotometer with sodium chloride prism. The majority of the preparations were studied in suspension in vaseline oil. The solutions were prepared in dichloroethane (the solvent was dried and distilled twice over calcium chloride); the concentrations ranged from 0.5×10^{-2} to 1.0×10^{-2} mole. The thickness of the solution layer was 0.5 mm. For proof that the concentrations of the substances were low enough to break up all intermolecular hydrogen bonds, solutions were also prepared with concentrations several times lower, and cuvettes were selected with correspondingly greater thickness of the layer; under these conditions the position of the maxima was unchanged, but the intensity of the bands was reduced rapidly. The solution concentrations proved to be insufficient in some cases, but this was caused by the limited solubility of the substances in dichloroethane. The dichloroethane proved to be the only suitable solvent for preparing the solutions (with respect to solubility of the imines and transparency of the medium in the required frequency zones).

Compounds for Investigation. Compounds (I), (VI), and (VIII) - (XIII) were synthesized in accordance with [6]. Compounds (II) and (IV) were obtained in accordance with [36]. The remaining compounds were obtained by various methods: (V) and (VII) according to [37], (XIV) according to [38], (XVI) and (XVIII) according to [39], (XVII) according to [40]. The 2,3-diphenylindone (XV) was obtained by a more complex method (see further).

1-Benzamido-2,3-diphenyl-3-hydroxyindene. A 2-g quantity of 2-phenyl-3-benzamidoindone [(E), $\text{R} = \text{C}_6\text{H}_5$] (see also [6]) was dissolved with heating in 70 ml of dry benzene. The solution was cooled, and the resulting paste was added in small portions to a solution of phenylmagnesium iodide (prepared from 1 g of magnesium in 20 ml of absolute ether and 6 g bromobenzene in 10 ml of ether). A violet precipitate was formed and dissolved immediately. The mixture was refluxed in a water bath for half an hour. The solution was decomposed with dilute hydrochloric acid, and the ether layer was separated, dried with sodium sulfate, and slowly evaporated. After a week it was filtered and dried. Yield 1.62 g. After crystallization from benzene the substance had two melting points: 105° and $215\text{--}216^\circ$.

Found %: N 3.72. $C_{23}H_{21}O_2N$. Calculated %: N 3.47.

The substance was soluble in the usual organic solvents. Its structure was proved by measuring infrared spectra. It had the following bands: δ_{NH} 1510, 1580 cm^{-1} ; $\nu_{C=C}$ 1602 cm^{-1} (vibrations of double bonds in the benzene ring); $\nu_{C=O}$ (amide) 1648 cm^{-1} ; ν_{OH} or ν_{NH} at 3170 cm^{-1} . There were no bands above 1700 cm^{-1} ; this proved that the Grignard reagent reacted just with the carbonyl group of the five-membered ring [(E), $R = C_6H_5$].

2,3-Diphenylindone (XV). A solution of 0.15 g of 1-benzamido-2,3-diphenylhydroxyindene in 7 ml of alcohol and 3 ml of concentrated hydrochloric acid was boiled for half an hour. Bright red crystals were separated; yield 0.09 g (86 %). M.p. 149-150.5° (from alcohol). Literature data: m.p. 151-152° [41]. Ammonia was detected in the filtrate after separation of the 2,3-diphenylindone.

2-Methyl-3-phenylaminindone (III). A solution of 4.6 g of methylindandione and 2 g of aniline in 10 ml of alcohol was boiled for three hours. After cooling, the reaction mixture congealed to a viscous mass. An orange, finely crystalline substance was separated out and washed with 50% alcohol. Yield 3.5 g; m.p. 188-189° (from glacial acetic acid and twice from alcohol).

Found %: N 6.27. $C_{16}H_{13}ON$. Calculated %: N 5.95.

Bright-red needles; soluble in the usual organic solvents; hydrolyzed by acids to aniline and methylindandione. This substance has been described previously [42], but then it had m.p. 153°. At present we have not been successful in obtaining such a substance.

SUMMARY

1. Infrared absorption spectra have been obtained for imines of 2-substituted indandiones and a number of other substances.
2. It has been demonstrated that 3-phenylaminindones in the solid form and in solution have the ketoenamine structure.
3. Unsubstituted imines in the solid form have primarily the iminoenol structure; in dichloroethane solution part of the molecules are converted to the ketoenamine form.
4. All of the compounds investigated which have even one atom of hydrogen on the nitrogen exhibit strong intermolecular association.
5. For benzoylated imines of 2-methyl- and 2-phenylindandione, acylated ketoenamine structures were demonstrated.

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METHYLFLUOROARYLCHLOROSILANES

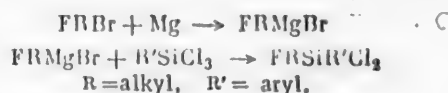
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Fluorine derivatives of arylchlorosilanes have been little studied. A few representatives of this class of compounds have been described in the literature. Thus, for example, trifluoromethylphenyltrichlorosilane and bis-(trifluoromethylphenyl) dichlorosilane [1-3] were obtained through organomagnesium compounds. Later, p-fluorophenyltrichlorosilane and bis(p-fluorophenyl)dichlorosilane have been obtained [4,5]. Recently, by interaction of fluorobenzene with methyldichlorosilane, a mixture of isomers of methylfluorophenyldichlorosilane [6] has been obtained with 18% yield.

In the present work, synthesis of certain representatives of the fluoroarylchlorosilanes has been accomplished, and their reactions with ethanol have been studied. Preparation of the fluoroarylchlorosilanes was carried out according to the following reaction:



p-Fluorophenylmagnesium bromide and o- and p-fluorobenzylmagnesium bromides were obtained by this reaction.

Experiments showed that despite the high yield of organomagnesium compound (95-96%), the yields of the products obtained, i.e., methyl-p-fluorophenyldichlorosilane, methyl-p-fluorophenylchlorosilane, methyl-o-fluorobenzylchlorosilane, and methyl-p-fluorobenzylchlorosilane, did not exceed 40-45%.

At the same time, there was always formed a considerable quantity of di(fluoroaryl)methylchlorosilanes and other reaction products which could not be separated successfully. The new compounds which we isolated were characterized; their properties are shown in Table 1.

From the compounds synthesized, methylfluoroarylethoxysilanes were obtained according to the scheme



The reaction was carried out by passing the reactants through a tube packed with glass Raschig rings at 60°. These conditions minimized the side reactions which usually develop during the esterification of alkyl- and arylhalosilanes as a result of the formation of water, hydrogen chloride, and alcohol. Thus there were obtained methyl-p-fluorophenyldiethoxysilane, methyl-o-fluorobenzylchlorosilane, and methyl-p-fluorobenzylchlorosilane with yields reaching 45%. The properties of the methylfluoroarylethoxysilanes which were obtained are shown in Table 2.

EXPERIMENTAL

Methyl-p-fluorophenyldichlorosilane. A 48-g quantity of magnesium, 200 ml of absolute ether, and 1 ml

TABLE 1

Substance	Boiling point	d_4^{20}	n_D^{20}	MR_D	
				found	calculated
Methyl-p-fluorophenyl-dichlorosilane (I)	196—198°	1.2502	1.5050	49.58	49.45
Methyl-p-fluorophenyl-chlorosilane (II)	177—178	1.1149	1.4960	45.71	45.39
Methyl-p-fluorobenzyl-dichlorosilane (III)	222—223	1.2384	1.5050	53.41	53.67
Methyl-o-fluorobenzyl-dichlorosilane (IV)	216—216.5	1.2328	1.5036	53.54	53.67

TABLE 2

Substance	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D	
				found	calculated
Methyl-p-fluorophenyl-diethoxysilane (V)	117—119° (32)	1.0240	1.4590	60.93	61.25
Methyl-p-fluorobenzyl-diethoxysilane (VI)	126—127 (21)	1.019	1.4640	65.55	65.47

of ethyl iodide were placed in a two-liter flask fitted with a reflux condenser, stirrer with liquid seal, dropping funnel, and nitrogen supply tube. A quantity of 324 g of fluorobromobenzene in 900 ml of absolute ether was added from the dropping funnel over 4 hours, with the stirrer in operation. After the addition, the reaction mixture was heated for 3 hours on a water bath. During each experiment dry purified nitrogen was supplied to the flask. A quantity of 500 ml of toluene was added to the prepared Grignard reagent, and 600–700 ml of the ether was boiled off on a water bath. Then the flask was closed with a stopper fitted with a calcium chloride drying tube and cooled rapidly to 20°. The cooled solution was decanted into a dropping funnel. The Grignard reagent was added from the dropping funnel, over 1.5 hours with stirring, to a solution of 350 g methyltrichlorosilane in 500 ml toluene. During the addition the reaction temperature rose to 50–60°, but then decreased gradually to 20°. After standing for 12 hours, the reaction mixture was stirred for 5 hours at room temperature and 3 hours with heating on a steam bath. Then the unreacted methyltrichlorosilane, toluene, and ether were distilled from a flask equipped with a dephlegmator, and the resulting (I) was separated by fractionation in a column with 10-theoretical-plate efficiency. Yield 115 g (42.5%). B.p. 196–198° (758 mm), d_4^{20} 1.2502, n_D^{20} 1.5050, MR_D 49.58; Calc. 49.45.

By esterification of (I), methyl-p-fluorophenyldiethoxysilane (V) was obtained. B.p. 117–119° (32 mm), 104° (15 mm), 140° (50 mm), d_4^{20} 1.0240, n_D^{20} 1.4590, MR_D 60.93; Calc. 61.25.

Found %: C 57.96, 58.07; H 7.38, 7.43; F 8.12, 8.10; C_2H_5O 38.93. $C_{11}H_{17}O_2SiF$. Calculated %: C 57.88; H 7.50; F 8.32; C_2H_5O 39.21.

Methyl-p-fluorophenylchlorosilane (II) was synthesized similarly to (I) from methyldichlorosilane and p-fluorobromobenzene, and had the following constants: b.p. 177–178° (755 mm), d_4^{20} 1.1149, n_D^{20} 1.4960, MR_D 45.71; Calc. 45.39.

Found %: C 47.68; H 4.8; Si 17.18; Cl 20.9. C_7H_9SiFCl . Calculated %: C 48.14; H 4.62; Si 16.03; Cl 20.32.

Methyl-p-fluorobenzyl-dichlorosilane (III). In a liter four-necked flask (fitted with reflux condenser, dropping funnel, stirrer with liquid seal, and thermometer) 7.9 g of magnesium and 100 ml of absolute ether were heated on a water bath; a solution of 58 g of p-fluorobenzyl bromide in 200 ml of ether was added from the dropping funnel. When the Grignard reaction had started, heating was discontinued and the reaction rate was controlled by

the rate of introduction of the p-fluorobenzyl bromide solution. After adding all the fluorobenzyl bromide, the reaction mixture was heated on a water bath for 2 hours, then cooled to room temperature and transferred by siphoning into a flask containing 100 g of methyltrichlorosilane; the Grignard reagent was added with cooling so that the temperature did not exceed 15°. After adding all the Grignard reagent the temperature was increased to 20°, and the contents of the flask were stirred for 1 hour and allowed to stand for 14 hours. Then the reaction mixture was heated on a water bath for 3 hours, cooled to room temperature, and decanted into a flask for distillation. The ether and the unreacted methyltrichlorosilane were distilled from the flask with a dephlegmator, and the resulting substance (III) was separated by fractionation in a column. Yield 35.5 g (52%). B.p. 222-223° (758 mm), d_4^{20} 1.2384, n_D^{20} 1.5050, MR_D 53.41; Calc. 53.67.

Found %: C 42.85; H 4.27; F 8.55. $C_8H_9SiFCl_2$. Calculated %: C 43.05; H 4.03; F 8.52.

Esterification of (III) gave (VI): b.p. 126-127° (21 mm), d_4^{20} 1.0198, n_D^{20} 1.4640, MR_D 65.55; Calc. 65.47.

Found %: C 58.9, 59.5; H 7.94, 8.27; F 7.42, 7.77. $C_{12}H_{13}O_2SiF$. Calculated %: C 59.47; H 7.90; F 7.84; C_2H_5O 37.13.

Methyl-o-fluorobenzyl-dichlorosilane (IV) was obtained by the same method as that used for (III). Yield 64.1 g (46.4%). B.p. 216-216.5° (753 mm), d_4^{20} 1.2328; n_D^{20} 1.5036; MR_D 53.54; Calc. 53.67.

Found %: C 43.93; H 4.37; F 8.54. $C_8H_9SiFCl_2$. Calculated %: C 43.05; H 4.03; F 8.52.

Esterification of methyl-p-fluorophenylchlorosilane (II) gave a substance (V) containing 38.96% C_2H_5O , with the following constants: b.p. 117-119° (32 mm), d_4^{20} 1.0240, n_D^{20} 1.4590.

SUMMARY

New compounds have been synthesized: methyl-p-fluorophenyl-dichlorosilane, methyl-p-fluorophenylchlorosilane, methyl-p-fluorobenzyl-dichlorosilane, and methyl-o-fluorobenzyl-dichlorosilane. The reaction of their conversion to ethoxy derivatives has been studied.

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INITIATED LIQUID-PHASE OXIDATION OF DIBENZYL

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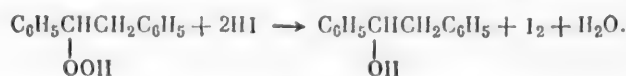
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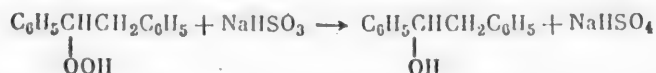
The present work is aimed at preparation and study of dibenzyl hydroperoxide, which has not been described in the literature. In particular, it was proposed to develop a technical method of preparing stilbene through dibenzyl hydroperoxide; presently known methods of obtaining stilbene [1-4] are suitable only as laboratory preparations.

It was proposed to obtain dibenzyl hydroperoxide by autooxidation of dibenzyl with molecular oxygen in the presence of manganese resinate, which has been applied successfully as an initiator in the processes of oxidizing ethylbenzene and isopropylbenzene [6]. However, oxidation experiments with even the very minimum quantities of manganese resinate showed that cleavage of the dibenzyl molecule occurred, with the formation of single-ring products (benzoic acid, benzaldehyde, and benzyl alcohol). Nevertheless, both the accumulated experience in the literature on the autooxidation of hydrocarbons and theoretical explanations of the mechanism of oxidation processes [5] convinced us that all the single-ring products detected upon oxidation of dibenzyl in the presence of manganese resinate are only products of decomposition of the initially formed dibenzyl hydroperoxide. We attempted to introduce small quantities (a few drops) of cumene hydroperoxide as an initiator of the oxidation reaction. The experiment showed that with such a method of oxidation it is possible to accumulate up to 25-26% dibenzyl hydroperoxide in the reaction mixture.

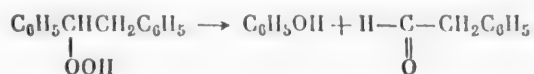
From the oxidized reaction mixture after preliminary extraction of benzoic acid through the sodium salt, dibenzyl hydroperoxide was separated and identified. After recrystallization from petroleum ether the hydroperoxide appeared in the form of colorless crystals with m.p. 52-53°. The substance is adequately stable under normal conditions and does not detonate with shock, introductions into a flame, etc. Upon heating much above the melting point it begins to decompose with evolution of dense fumes with a phenol odor. With acidic solutions of potassium iodide in glacial acetic acid it reacts quantitatively according to the equation



The indicated reaction can be utilized for quantitative determination of the hydroperoxide. Upon careful reduction in benzene solution by sodium bisulfite the hydroperoxide is converted to phenyl benzyl carbinol.



The decomposition of dibenzyl hydroperoxide at 25-40° in benzene solution by means of concentrated sulfuric acid leads mainly to the formation of phenol and phenylacetaldehyde.



At the same time, trans-stilbene is formed (as a result of dehydration of phenyl benzyl carbinol).

EXPERIMENTAL

The dibenzyl had b.p. 148-150° (15 mm); after solidification, m.p. 50-52°.

Autooxidation of Dibenzyl in the Presence of Manganese Resinate

Into a four-necked cylindrical glass reactor, equipped with a mechanical stirrer, there was introduced 60 g of dibenzyl and 0.6 or 0.07 g (first and second experiments, respectively) of manganese resinate. The reactor contents were heated to 110°, after which mechanical agitation was started and air was fed in by means of a bubbler (drawn-out glass tube reaching to the bottom of the reactor). The air bubbling rate was held at about 4 liters/hr. The oxygen absorbed from the air was checked by means of two flowmeters (at inlet and outlet). Samples of the reaction mixture were withdrawn periodically and at the end of the experiment for iodometric determination of hydroperoxide content. At the end of the experiment the cooled reaction mixture was dissolved in an equal weight of benzene, and after establishing the absence of hydroperoxide it was subjected to further treatment for separation of the reaction products.

Benzoic acid was separated by treating the benzene solution with a 10% sodium carbonate solution and subsequently acidifying the sodium carbonate extract with hydrochloric acid. The benzoic acid (which came out in the precipitate) was washed and recrystallizing from hot water melted at 120°, and upon mixing with a known sample of benzoic acid did not give any melting-point depression.

Benzaldehyde was separated by the usual method in the form of bisulfite compounds with subsequent decomposition by sodium carbonate. An oil with a bitter almond odor distilled in the form of a colorless liquid at 177-180°. The semicarbazone melted at 212° (without recrystallization).

Benzyl alcohol was separated (after removal of benzaldehyde and benzene) by fractionating the residue. An oily liquid with an aromatic odor was obtained, distilling at 200-207°. Literature data for benzyl alcohol: b.p. 205.5°. The results of the experiments are shown in Table 1.

TABLE 1

Products obtained (g)			Separated from reaction mixture (g)			
in reactor	in trap	total	benzoic acid	benzaldehyde	benzyl alcohol	dibenzyl
62.3	1.3	63.6	12.5	1.8	2.1	24.3
62.1	0.7	62.8	7.55	0.1	—	35.1

Oxidation of Dibenzyl in the Absence of Metallic Initiator

The conditions of the experiments were the same as in the preceding section. The "primer" of cumene hydroperoxide (a few drops) was introduced into the reactor before starting the air flow. The reaction mixture was analyzed for content of dibenzyl hydroperoxide (iodometrically) and of benzoic acid. Results of the experiments are shown in Table 2.

Upon dilution of the reaction mixture with benzene, first the benzoic acid was extracted. Then the benzene solution of the oxidized mixture was cooled to 0° and the dibenzyl hydroperoxide occurring in it was extracted by a 25% sodium hydroxide solution in the form of the hydrated sodium salt $C_6H_5CH(OONa)CH_2C_6H_5 \cdot x H_2O$, similarly to the hexahydrate of the sodium salt of cumene hydroperoxide [6]. After vacuum filtration in a Schott filter, washing gently with benzene, and air drying, the salt of the hydroperoxide was dissolved in water, and the solution was saturated with excess carbon dioxide; thereupon the solution became completely transparent, and in a day a crystalline mass of the free dibenzyl hydroperoxide was precipitated. After washing the precipitated hydroperoxide with water and recrystallizing from petroleum ether, it appeared in the form of snow-white prisms, melting at 52-53°; a mixed sample with dibenzyl gave a sharp melting-point depression. The crystals were readily soluble in ether, benzene, or glacial acetic acid, insoluble in water, and difficultly soluble in cold petroleum ether. Upon addition of a drop of concentrated sulfuric acid to a small quantity of the hydroperoxide in a test tube, immediate ignition and a white cloud with phenol odor were observed.

Dibenzyl charged (g)	Length of experiment (hr)	Oxygen absorbed (liters)	Reaction mixture obtained (g)	Content in reaction mixture (%)	
				dibenzyl hydroperoxide	benzoic acid
90	33	9.6	91.5	22.20	1.03
90	35	10.6	92.4	20.00	1.63
120	27	7.5	115.0	26.60	0.64
120	28.5	10.0	118.0	20.00	0.47
129	34	7.0	128.5	23.80	0.42
120	31	8.0	120.5	21.31	1.27
152	40	10.0	153.0	22.20	0.54

Found %: C 78.23; H 7.07; active oxygen 7.29, 7.03. $C_{14}H_{14}O_2$. Calculated %: C 78.46; H 6.60; active oxygen 7.47.

These data permit the assertion that the substance which we have isolated is the monohydroperoxide of dibenzyl, which is still undescribed in the literature.

Action of Concentrated Sulfuric Acid on Dibenzyl Hydroperoxide

Concentrated sulfuric acid (2 drops per gram of hydroperoxide) was added cautiously dropwise to a benzene solution of the hydroperoxide, with vigorous mechanical agitation and cooling. Upon completion of the sulfuric acid addition, the mixture was warmed to 40° with the stirrer operating, until disappearance of the hydroperoxide reaction. After neutralizing the mixture with powdered potassium carbonate, the phenol which was formed was extracted by the usual method, by means of sodium hydroxide, subsequent acidification with hydrochloric acid, and extraction of the phenol by ether. The recovered phenol distilled at 70-80° (3 mm) and immediately solidified in colorless crystals with the characteristic phenol odor. The benzoate melted at 67-68°. The yield of phenol was 38%. Phenylacetaldehyde was extracted from the mixture (after removing the phenol and distilling off the benzene) by vacuum distillation of the residue at 70-90° (3 mm), in the form of a colorless oil with hyacinth odor. The semicarbazone melted at 150°. Further distillation of the residue within the limits of 160-170° (3 mm) gave a substance which crystallized immediately in the form of colorless crystals melting at 118°; upon mixing with a known sample of stilbene, no melting-point depression was observed.

Reduction of Dibenzyl Hydroperoxide by Sodium Bisulfite Solution

To a solution of dibenzyl hydroperoxide in 5 parts of benzene, stirred vigorously and cooled (within limits of 15-23°), there was added gradually a 40% aqueous solution of sodium bisulfite (150% of the theoretical quantity). Stirring was continued until disappearance of the hydroperoxide reaction. The aqueous and benzene layers were isolated from the precipitated sediment of bisulfite and then were separated in a separatory funnel. Unexpectedly, the principal reaction product proved to be in the aqueous layer, from which it was recovered by acidification with hydrochloric acid and subsequent extraction by ether. Upon removal of the ether, the residue crystallized. After recrystallization from dilute methanol the substance appeared in the form of delicate colorless needles with m.p. 64-65°, which agrees with the literature data for phenyl benzyl carbinol. Then from the benzene solution, upon removal of the benzene, a fraction was collected distilling up to 146° (2 mm), which immediately crystallized in the receiver and after recrystallization from ethanol appeared in the form of colorless brilliant needles which melted at 118° and did not give any melting-point depression in a mixed sample with known stilbene. The formation of stilbene evidently takes place either in the process of reduction itself, or is accomplished by dehydration of that part of the phenyl benzyl carbinol which remains dissolved in the benzene layer, in the course of the vacuum distillation.

SUMMARY

1. The oxidation of dibenzyl by atmospheric oxygen in the presence of manganese resinate proceeds with cleavage of the dibenzyl molecule; thereby there are formed benzyl alcohol, benzaldehyde, and benzoic acid.
2. Oxidation of dibenzyl in the absence of metallic impurities, oxides, or salts of heavy metals leads to the formation of dibenzyl hydroperoxide.

3. Under the action of sulfuric acid, dibenzyl hydroperoxide is decomposed to phenol and phenylacetaldehyde.

4. Dibenzyl hydroperoxide is reduced by sodium bisulfite to phenyl benzyl carbinol; stilbene may be obtained by dehydration of the latter.

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BIPOLAR IONS FORMED UPON SPLITTING A PROTON FROM AN NH- GROUP

XVI. REARRANGEMENT OF BIPOLAR IONS OF THE STILBENE SERIES

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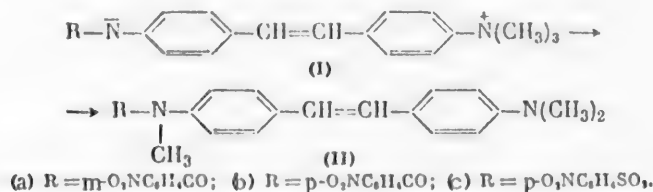
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Betaines of the benzene series which are formed by splitting a proton from an NH- group are subject to rearrangement upon melting; in such rearrangement a methyl group is split from the onium atom in the form of a cation and is added to the azeniate N-atom [1, 2].

We found that similarly formed bipolar ions of the stilbene series (I) also can undergo this type of rearrangement [3]. Although the cationic and anionic* centers in the molecule of these betaines are much farther apart than in the benzene derivatives studied previously, in the given case the rearrangement also proceeds very readily with the formation of (II). This observation makes it possible to assume that the given reaction is an intermolecular conversion.



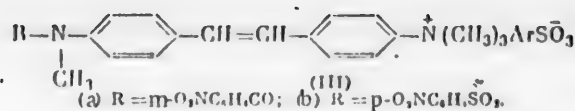
The betaine (Ia) undergoes rearrangement upon melting (190°). In the case of the high-melting betaines (Ib) and (Ic) it is more expedient to conduct the process in naphthalene medium: The reaction occurs at a lower temperature and with considerably higher yields.

The rearrangement product is also formed upon melting the betaine (Ic) in β -naphthol medium; under these conditions the betaine (Ib) reacts with the β -naphthol, converting it to nerolin [methyl β -naphthyl ether]. The influence of the nature of the acyl radical upon the direction of the reaction occurring in the presence of β -naphthol was examined earlier in a study of the conversions of betaines of the sulfonium series [2].

The structure of the rearrangement products which were obtained was proved by means of the following conversions. Upon methylation of 4-p-nitrobenzenesulfamino-4'-dimethylaminostilbene by means of dimethyl sulfate, a compound was formed which was identical with (IIc). That same substance was obtained upon interaction of p-nitrobenzenesulfonyl chloride with the diamine formed upon hydrolysis of (IIb); hence, this diamine is 4-methylamino-4'-dimethylaminostilbene, and the compound (IIb) is its p-nitrobenzoyl derivative.

Upon melting the betaines (Ia) or (Ic) with the methyl ester of an arylsulfonic acid, a reaction occurred which is analogous to the conversions described previously for certain betaines of the quinoline [4] and pyridino-glyoxaline series [5], also leading to the formation of quaternary salts (III). Those same compounds were obtained starting from the rearrangement products of the betaines, which serves as proof of their structure.

*Owing to the redistribution of electron density caused by the influence of electron-acceptor groups, the azeniate N-atom carries only a part of the anionic charge.



The betaines containing the nitrobenzoic acid radical evidently have the greater part of the anionic charge located on the oxygen atom of the acyl group; in this case both rearrangement and alkylation of the betaines take place with migration of the reaction center.

EXPERIMENTAL

4-(N-Methyl-m-nitrobenzoylamino)-4'-dimethylaminostilbene (IIa). A test tube containing 0.55 g of the methylbetaine of 4-m-nitrobenzoylamino-4'-dimethylaminostilbene (Ia) was placed in an oil bath at 180°, and the temperature was increased slowly. The melt which was formed was heated at 190° for 5 minutes and then cooled. The rearrangement product formed light brown plates with m. p. 167-168° (from aqueous pyridine), difficultly soluble in alcohol or benzene. Yield 0.45 g (81%).

Found %: C 71.78, 71.78; H 5.67, 6.03; N 10.30, 10.52. $\text{C}_{24}\text{H}_{23}\text{O}_3\text{N}_3$. Calculated %: C 71.79; H 5.77; N 10.47.

Methylbenzenesulfonate of 4-(N-methyl-m-nitrobenzoylamino)-4'-dimethylaminostilbene (IIIa). The compound was formed upon melting the methylbetaine of 4-m-nitrobenzoylamino-4'-dimethylaminostilbene or the product of its rearrangement (IIa) with a slight excess of the methyl ester of benzenesulfonic acid at 60-70°. Pale yellow plates (from water with m. p. 235-236° (decomp.)).

Found %: N 7.31, 7.11. $\text{C}_{31}\text{H}_{31}\text{O}_6\text{N}_3\text{S}$. Calculated %: N 7.32.

4-(N-Methyl-p-nitrobenzoylamino)-4'-dimethylaminostilbene (IIb). A mixture of 0.4 g of the methylbetaine of 4-p-nitrobenzoylamino-4'-dimethylaminostilbene (Ib) and 0.4 g of naphthalene was heated in an oil bath. At 185° a transparent melt was formed. After 5 minutes it was cooled and triturated with ether. The residue was filtered off and washed with ether. Dark brown needles (from toluene) with m. p. 235-236°, difficultly soluble in alcohol or benzene. Yield 0.35 g (87%). In the absence of naphthalene the rearrangement took place upon melting the betaine (m. p. 216-218°), accompanied by tar formation (product yield 35%).

Found %: N 10.58, 10.74. $\text{C}_{24}\text{H}_{23}\text{O}_3\text{N}_3$. Calculated %: N 10.47.

Interaction of methylbetaine of 4-p-nitrobenzoylamino-4'-dimethylaminostilbene with β -naphthol. A mixture of 0.4 g of the betaine and 0.2 g of β -naphthol was heated in an oil bath at 160°. The red viscous mass which was formed was held at 160° for 5 minutes, cooled, and triturated with ether. The residue was filtered off and crystallized from aqueous pyridine. Red crystals, m. p. 285-286°, representing 4-p-nitrobenzoylamino-4'-dimethylaminostilbene. Yield 0.36 g (92%). From the ether solution, the methyl ether of β -naphthol was recovered with a yield of 0.13 g (87%).

4-Methylamino-4'-dimethylaminostilbene. A solution of 1.6 g of 4-(N-methyl-p-nitrobenzoylamino)-4'-dimethylaminostilbene in 50 ml of hydrochloric acid (1:1) was heated in a water bath for 2 hours and then boiled gently for 1 hour. The precipitate of p-nitrobenzoic acid which formed upon cooling (0.4 g) was filtered off. The filtrate was made alkaline, the amine was extracted by ether, and the ether was distilled off. Needle-like crystals (from propanol); m. p. 175-177°; soluble in benzene or ether, difficultly soluble (with heating) in alcohol. Yield 0.92 g (91%).

Found %: N 10.93, 10.94. $\text{C}_{17}\text{H}_{20}\text{N}_2$. Calculated %: N 11.10.

4-(N-Methyl-p-nitrobenzenesulfamino)-4'-dimethylaminostilbene (IIc). a) The compound was formed upon rearrangement of the methylbetaine of 4-p-nitrobenzenesulfamino-4'-dimethylaminostilbene (Ic). The reaction was carried out in naphthalene medium at 170°. Dark red needles (from xylene) with m. p. 217-218°; readily soluble in pyridine, difficultly soluble in benzene or alcohol. Yield 90%. In the absence of naphthalene the reaction took place at 220° with 54% yield.

Found %: N 9.71, 9.61. $\text{C}_{23}\text{H}_{23}\text{O}_4\text{N}_3\text{S}$. Calculated %: N 9.60.

* Taking into account the conditions under which the stilbene derivatives were obtained (described previously [3] and in the present communication), it may be assumed that these compounds are trans-forms.

The rearrangement also took place upon melting the betaine in β -naphthol medium at 150°. Yield 95%. Alkylation [formation of the ether] of the β -naphthol was not observed.

b) The sodium derivative of 4-p-nitrobenzenesulfamino-4'-dimethylaminostilbene was heated in alcohol medium, a slight excess of dimethyl sulfate was introduced, and the mixture was boiled for 45 minutes. Upon cooling, a precipitate formed. Dark red needles (from xylene) with m.p. 217-218°.

c) The compound was also formed upon heating (95°, 2 hours) 4-methylamino-4'-dimethylaminostilbene (0.30 g) with p-nitrobenzenesulfonyl chloride (0.26 g). Yield 0.41 g (79%). M. p. 217-218°.

Mixed melting point tests showed that the products obtained in (a), (b), and (c) were identical.

Methyl-p-toluenesulfonate of 4-(N-methyl-p-nitrobenzenesulfamino)-4-dimethylaminostilbene (IIb). The methylbetaine of 4-p-nitrobenzenesulfamino-4'-dimethylaminostilbene or the product of its rearrangement was melted with a slight excess of the methyl ester of p-toluenesulfonic acid at 120°. Yellow plates (from alcohol-ether mixture) with m. p. 268-269° (decomp.).

Found %: N 6.71, 6.63. $C_{13}H_{13}O_7N_3S_2$. Calculated %: N 6.74.

SUMMARY

1. Betaines of the stilbene series which are formed by splitting a proton from an NH- group undergo rearrangement upon melting, ending in the shift of a methyl group from the onium atom to the azeniate N-atom. The reaction proceeds smoothly in naphthalene medium.

2. Betaines of this series combine with the methyl ester of an arylsulfonic acid, forming quaternary salts.

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AZO DYES ON THE BASIS OF DIMETHYL ESTERS OF AMINOPHENYLSULFONAMIDOPHOSPHORIC ACIDS

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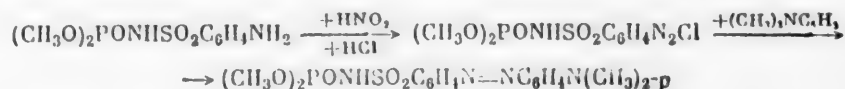
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The literature describes N^4 -derivatives of sulfanilamide and phosphoric acid of the type $p\text{-RR'NSO}_2\text{C}_6\text{H}_4\cdot\text{NHPC(NRR')}_2$ obtained by T. Bieber and B. Kane [1], and N^1 -derivatives of the type $p\text{-(RO)}_2\text{FONHSO}_2\text{C}_6\text{H}_4\text{NH}_2$, which we obtained recently [2].

Azo dyes on the basis of dimethyl esters of aminophenylsulfonamidophosphoric acids are also N^1 -derivatives of sulfanilamides and phosphoric acid, and therefore are of interest as possible physiologically active substances. Azo dyes of this type were obtained successfully by diazotization of the dimethyl esters of aminophenylsulfonamidophosphoric acids [2] and coupling the resulting diazonium salts with phenol, β -naphthol, or dimethylaniline.

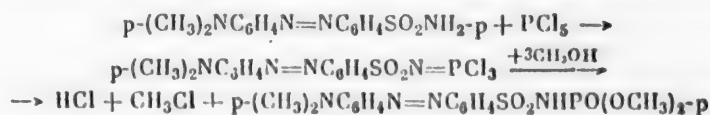


Diazotization of the dimethyl esters of aminophenylsulfonamidophosphoric acids was carried out in aqueous hydrochloric acid solutions under the usual conditions. Coupling with phenol or β -naphthol was carried out in alkaline medium (for coupling with dimethylaniline, in acidic medium), also under the usual conditions.

The dimethyl esters of p -hydroxybenzeneazo- o -, m -, and p -benzenesulfonamidophosphoric acids (I) and the dimethyl esters of β -naphtholazo- o -, m -, and p -benzenesulfonamidophosphoric acids (II) are crystalline substances, readily soluble in hot water and difficultly soluble in cold water, with weakly acidic character (see table). With aqueous sodium carbonate or sodium hydroxide solutions the esters (I) give sodium salts which are readily soluble in water, but the esters (II) give difficultly-soluble salts. The esters (I) are yellow in color, and the esters (II) are orange. The esters (I) and (II) dissolve in concentrated hydrochloric or sulfuric acid with a deepening of color.

The dimethyl esters of p -dimethylaminobenzeneazo- o -, m -, and p -benzenesulfonamidophosphoric acids (III) are crystalline substances with red color, readily soluble in hot water and difficultly soluble in cold water, with acidic character (see table). With aqueous sodium carbonate or sodium hydroxide solutions they give orange-colored crystalline sodium salts which are difficultly soluble in water. The esters dissolve in concentrated hydrochloric or sulfuric acid with a deepening of color.

The dimethyl ester of p -dimethylaminobenzeneazo- p -benzenesulfonamidophosphoric acid was also obtained from p -dimethylaminobenzeneazo- p -benzenesulfonamide through the corresponding trichlorophosphazone compound.



Azo Dyes of the Type $\text{ArN}=\text{NC}_6\text{H}_4\text{SO}_2\text{NHPO}(\text{OCH}_3)_2$ *

Position of $\text{ArN}=\text{N}-$	Ar	Yield, %	Melting point	λ_{max}	Transition interval of pH	Found N (%)	Empirical formula	Calculated N (%)	Solubility**				
									alcohol	ether	C_6H_6	CCl_4	petroleum ether
o	p-HOC ₆ H ₄	94	175—176°	Below 400	—	10.93, 10.91	$\text{C}_{14}\text{H}_{16}\text{O}_6\text{N}_3\text{SP}$	10.91	++	—	—	—	++
m	p-HOC ₆ H ₄	71	139—140	Below 400	—	10.74, 10.88	$\text{C}_{14}\text{H}_{16}\text{O}_6\text{N}_3\text{SP}$	10.91	++	—	—	—	++
p	p-HOC ₆ H ₄	72	174—175	404	—	10.59, 10.51	$\text{C}_{14}\text{H}_{16}\text{O}_6\text{N}_3\text{SP}$	10.91	+	—	—	—	++
o	2-HOC ₁₀ H ₆ -1	74	196—197	482	—	9.38, 9.40	$\text{C}_{18}\text{H}_{18}\text{O}_6\text{N}_3\text{SP}$	9.65	+	—	—	—	+
m	2-HOC ₁₀ H ₆ -1	60	175—178	478	—	9.73, 9.60	$\text{C}_{18}\text{H}_{18}\text{O}_6\text{N}_3\text{SP}$	9.65	+	+	+	—	++
p	2-HOC ₁₀ H ₆ -1	75	191—193	484	—	9.57, 9.71	$\text{C}_{18}\text{H}_{18}\text{O}_6\text{N}_3\text{SP}$	9.65	+	—	—	—	++
o	p-(CH ₃) ₂ NC ₆ H ₄	79	171—173	427	3.71—5.39***	13.44, 13.59	$\text{C}_{16}\text{H}_{21}\text{O}_3\text{N}_4\text{SP}$	13.59	++	—	—	—	—
m	p-(CH ₃) ₂ NC ₆ H ₄	73	182—184	422	3.73—4.60***	13.39, 13.26	$\text{C}_{16}\text{H}_{21}\text{O}_3\text{N}_4\text{SP}$	13.59	+	—	—	—	+
p	p-(CH ₃) ₂ NC ₆ H ₄	89****	193—194	432	3.71—5.27***	13.79, 13.59	$\text{C}_{16}\text{H}_{21}\text{O}_3\text{N}_4\text{SP}$	13.59	+	—	—	—	+

* All substances were crystallized from water or alcohol in the form of needles.

** + readily soluble at 20°C; + readily soluble at boiling point; — difficulty soluble at boiling point; = insoluble at boiling point. All substances: water +.

*** Index of titration pH 4.

**** Yield 86% from p-dimethylaminobenzenediazo-p-benzenesulfonamide.

The synthesis is of interest, since it is the first case of application of the phosphazo reaction for a relatively complex molecule containing a dimethylamino and an azo group; this broadens the limits of application of the phosphazo reaction. Samples of the esters obtained by the two different schemes described above have identical absorption maxima (432 $m\mu$) and identical melting points (193–194° C), and do not show any melting-point depression on a mixed sample; this proves that they are identical.

All of the azo dyes which were obtained are acid-base indicators. The esters (III) have an especially sharp color change. Therefore for these esters the interval of color change was determined, using a volume method (see table); this interval proved to be very close to the color change interval of methyl orange, and the index of titration proved to be identical with that of methyl orange (pH 4). The color change at the transition point is considerably more distinct than for methyl orange; therefore titration is accomplished easily and accurately with these new indicators, independent of the experimenter's color vision acuity.

Therefore, the esters (III) can be recommended as more nearly ideal indicators, for the replacement of methyl orange. The most suitable for this purpose is the dimethyl ester of p-dimethylaminobenzeneazo-p-benzenesulfonamidophosphoric acid, which is readily obtained from p-dimethylaminobenzeneazo-p-benzenesulfonamide, phosphorus pentachloride, and methanol.

EXPERIMENTAL

Dimethyl Esters of p-Hydroxybenzeneazo- and β -Naphtholazobenzenesulfonamidophosphoric Acids (see table). 0.005 mole quantity of the dimethyl ester of the aminophenylsulfonamidophosphoric acid dissolved in 5 ml of 5 N hydrochloric acid was diazotized, slowly adding 1 ml of 5 N sodium nitrite solution with ice water cooling of the reaction mixture. Completion of the diazotization was determined by iodine-starch paper (blue color). Then the diazonium salt solution was neutralized with sodium carbonate to weakly acidic reaction and rapidly mixed with a solution (cooled to 0°) of 0.005 mole of phenol (or β -naphthol) in 2.5 ml of 2 N sodium hydroxide solution. The mixture was allowed to stand 2–3 hours at room temperature and acidified with hydrochloric acid. This resulted in precipitation of the esters (I) or (II), which were filtered off by suction and recrystallized from water or alcohol.

Dimethyl Esters of p-Dimethylaminobenzeneazobenzenesulfonamidophosphoric Acids. These were obtained the same as the esters (I) or (II), except that the coupling was carried out in weakly acidic solution.

Dimethyl Ester of p-Dimethylaminobenzeneazo-p-benzenesulfonamidophosphoric Acid. A mixture of 0.02 mole of finely ground p-dimethylaminobenzeneazo-p-benzenesulfonamide, 0.02 mole of phosphorus pentachloride, and 75 ml of carbon tetrachloride was heated slowly with vigorous stirring, and was refluxed until hydrogen chloride evolution ceased (3 hours). Then, without stopping the stirrer, 200 ml of anhydrous methanol was added rapidly and stirring was continued for 1 hour. After 12 hours the solvent was removed by vacuum distillation, and the residue was recrystallized from water or alcohol; yield 86%.

The properties of this material were identical with those of the substance obtained by coupling the diazonium salt of the dimethyl ester of p-aminophenylsulfonamidophosphoric acid with dimethylaniline (see table).

SUMMARY

1. By coupling the diazonium salts obtained from dimethyl esters of aminophenylsulfonamidophosphoric acids with phenol, β -naphthol, or dimethylaniline, the corresponding azo dyes are formed; these have the properties of acid-base indicators.

2. The dimethyl ester of p-dimethylaminobenzeneazo-p-benzenesulfonamidophosphoric acid has the same index of titration as methyl orange, but has a color change at the transition point which is considerably more distinct than that of methyl orange.

The dimethyl ester of p-dimethylaminobenzeneazo-p-benzenesulfonamidophosphoric acid was also obtained by an alternate synthesis from p-dimethylaminobenzeneazo-p-benzenesulfonamide, through the corresponding trichlorophosphazo compound.

3. The phosphazo reaction for amides of sulfonic acids is applicable for substances whose molecules contain an azo and a dimethylamino group.

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* Original Russian pagination. See C. B. translation.

DIESTERS OF ACYLAMIDOPHOSPHORIC ACIDS

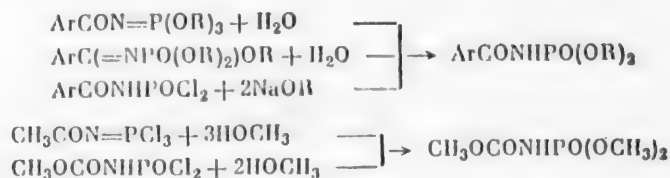
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Dieters of acylamidophosphoric acids are starting materials in obtaining various derivatives of phosphoric acid, for example acid chlorides* of N-dichloro-, N-dialkoxy-, and N-diaroxyphosphinyliminocarboxylic acids [1, 4], thio-derivatives of acylamidophosphoric acids [2], and many others. Up to the present time dieters of acylamidophosphoric acids have been obtained by hydrolysis of trialkoxy- and triaroxyphosphazacyls [3], by hydrolysis of acid chlorides and esters of N-dialkoxy- and N-diaroxyphosphinyliminocarboxylic acids [4], by the action of sodium alcoholates and arylates [phenolates] on acylamidophosphoric acid dichlorides [5], and in certain isolated cases by the action of excess alcohol on trichlorophosphazo compounds or acylamidophosphoric acid dichlorides [6], according to the following schemes:



In all of these cases, excluding the latter two special cases, in obtaining the dieters of acylamidophosphoric acids it is necessary to prepare dry phenolates or solutions of the alcoholates using metallic sodium, which has a number of disadvantages and is quite time-consuming.

As a result of numerous experiments it was found that aromatic dieters of acylamidophosphoric acids can be obtained with good yields directly from trichlorophosphazacyls and phenols in the presence of tertiary amines (pyridine, dimethylaniline, triethylamine), and the dimethyl esters can be obtained from trichlorophosphazacyls and a large excess of methanol (compare [6]). Using these methods, a number of dieters of acylamidophosphoric acids were obtained which are already described (Table 1) and several which are not described in the literature (Table 2).

*The names which we proposed previously [7, 4] for these types of compounds—trichloroisophosphazacyls [$\text{ArC}(=\text{NPOCl}_2)\text{Cl}$], C-chloro-p,p-diaroxyisophosphazacyls [$\text{ArC}(=\text{NPO}(\text{OAr}')_2)\text{Cl}$], trialkoxyisophosphazacyls [$\text{ArC}(=\text{NPO}(\text{OAlk})_2)\text{OAlk}$], and in general the term isophosphazacyls ($\text{ArC}=\text{NPO}$) we acknowledge as unfortunate, and consider that it is better to regard these compounds as derivatives of the hypothetical N-phosphinyliminocarboxylic acids [$\text{RC}(=\text{NPOH}_2)\text{OH}$], since thereby it is not necessary to introduce a new term (isophosphazacyls), and it is possible to give a clear and relatively simple name for the majority of the compounds of this type, for example the acid chlorides of N-dichlorophosphinyliminocarboxylic acids [$\text{RC}(=\text{NPOCl}_2)\text{Cl}$].

TABLE I
Diesters of Acylamidophosphoric Acids of the Type (RO)₂ PONHCO^a

R	R'	Yield, %	Literature reference	R	R'	Yield, %	Literature reference
CH ₃	C ₆ H ₅	97	[3]	C ₆ H ₅	3,5-(NO ₂) ₂ C ₆ H ₃	90	[3]
CH ₃	p-ClC ₆ H ₄	77	[3]	C ₆ H ₅	p-CH ₃ OC ₆ H ₄	70	•
CH ₃	m-NO ₂ C ₆ H ₄	98	•	C ₆ H ₅	CCl ₃	71	[3]
CH ₃	p-NO ₂ C ₆ H ₄	91	[3]	p-ClC ₆ H ₄	C ₆ H ₅	75***	[3]
CH ₃	3,5-(NO ₂) ₂ C ₆ H ₃	96	[3]	p-ClC ₆ H ₄	p-ClC ₆ H ₄	81	[3]
CH ₃	CCl ₃	82	[9]	p-ClC ₆ H ₄	p-BrC ₆ H ₄	81	•
C ₆ H ₅	C ₆ H ₅	99**	[3]	p-ClC ₆ H ₄	m-NO ₂ C ₆ H ₄	87	[10]
C ₆ H ₅	p-ClC ₆ H ₄	86	[3]	p-ClC ₆ H ₄	p-NO ₂ C ₆ H ₄	97	[3]
C ₆ H ₅	o-BrC ₆ H ₄	71	•	p-ClC ₆ H ₄	3,5-(NO ₂) ₂ C ₆ H ₃	91	[3]
C ₆ H ₅	p-BrC ₆ H ₄	79	•	p-NO ₂ C ₆ H ₄	C ₆ H ₅	87****	[3]
C ₆ H ₅	o-NO ₂ C ₆ H ₄	80	•	p-NO ₂ C ₆ H ₄	p-ClC ₆ H ₄	97	[3]
C ₆ H ₅	m-NO ₂ C ₆ H ₄	87	[10]	p-NO ₂ C ₆ H ₄	o-NO ₂ C ₆ H ₄	91	•
C ₆ H ₅	p-NO ₂ C ₆ H ₄	93	[3]	p-NO ₂ C ₆ H ₄	p-NO ₂ C ₆ H ₄	86	[3]

^a Not described in literature; for properties see Table 2.

• Upon decreasing quantities of phenol and pyridine to 2 moles, yield 73%.

•• Upon decreasing quantities of phenol and pyridine to 2 moles, yield 64%.

••• Upon decreasing quantities of phenol and pyridine to 2 moles, yield 75%.

•••• Upon decreasing quantities of phenol and pyridine to 2 moles, yield 75%.

TABLE 2

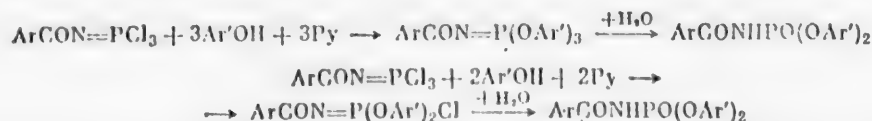
Diesters of Acylamidophosphoric Acids of the Type $(RO)_2PONHCOAr^*$

R	Ar	Melting point	Appearance	Found (%)	Empirical formula	Calculated (%)	Solubility ^{••}			
							benzene	alcohol	acetone	di-oxane
CH ₃	m-NO ₂ C ₆ H ₄	124—126°	Prisms (from alcohol)	N 10.07, 9.99	C ₉ H ₁₁ O ₈ N ₂ P	N 10.22	+	+	++	++
C ₆ H ₅	o-BrC ₆ H ₄	111—112	Prisms (from alcohol)	Br 18.70, 18.74	C ₁₉ H ₁₅ O ₅ NPBr	Br 18.49	+	+	++	++
C ₆ H ₅	p-BrC ₆ H ₄	132—133	Prisms (from alcohol)	N 3.13, 3.16; Br 18.63, 18.68	C ₁₉ H ₁₅ O ₄ NPBr	N 3.24; Br 18.49	—	—	+	+
C ₆ H ₅	o-NO ₂ C ₆ H ₄	121—122	Prisms (from alcohol)	N 6.93, 7.03	C ₁₉ H ₁₅ O ₆ N ₂ P	N 7.03	+	+	++	++
C ₆ H ₅	p-CH ₃ OC ₆ H ₄	131—133	Prisms (from methanol)	N 4.00, 4.06	C ₂₀ H ₁₈ O ₅ NP	N 3.67	+	+	++	++
p-ClC ₆ H ₄	p-BrC ₆ H ₄	151—152	Prisms (from alcohol—dioxane mixture)	N 2.67, 2.69; (Cl + Br) 29.82, 30.21	C ₁₉ H ₁₃ O ₄ NP(Cl ₂ Br)	N 2.79; (Cl + Br) 30.10	—	—	+	+
p-NO ₂ C ₆ H ₄	o-NO ₂ C ₆ H ₄	168—169	Prisms (from alcohol—dioxane mixture)	N 11.20, 11.30	C ₁₉ H ₁₃ O ₁₀ N ₄ P	N 11.47	—	—	—	+

[•] Yields—see Table 1.^{••} All compounds were insoluble (at the boiling point) in water, petroleum ether, ether, or carbon tetrachloride. † readily soluble at 20°;

+ readily soluble at boiling point; —difficultly soluble at boiling point.

The formation of the diesters of acylamidophosphoric acids from trichlorophosphazoyls and phenols in the presence of tertiary bases can proceed by two different schemes:



Apparently the reaction goes according to Scheme (I), since upon decreasing the quantity of phenol to 2 moles per mole of trichlorophosphazoyl the yield of diesters is reduced considerably. Evidently, in the presence of tertiary amines the reaction rate of the phenols with the diaroxychlorophosphazoyls is greater than the reaction rate of the phenols with aroxydichlorophosphazoyls or trichlorophosphazoyls. Therefore, upon decreasing the quantity of phenol there is formed a mixture of triaroxyphosphazoyls and diaroxychlorophosphazoyls (which upon hydrolysis give the diesters) with aroxydichlorophosphazoyls and trichlorophosphazoyls (which upon hydrolysis give water-soluble compounds), thus decreasing the yields markedly.

For obtaining the dimethyl esters of acylamidophosphoric acids, the corresponding trichlorophosphazoyl was added to a large excess of methanol (1 mole in 0.8–1.0 liter), the reaction mixture was allowed to stand for 2–2.5 hours at room temperature, and the methanol was removed by vacuum distillation. The reaction proceeds almost quantitatively according to the following scheme (compare [6]):



EXPERIMENTAL

Dimethyl Esters of Acylamidophosphoric Acids. The trichlorophosphazoyl (0.1 mole) was added with cooling and stirring to methanol (80–100 ml) at such a rate that the temperature of the reaction mixture did not rise above 15°C. Then the mixture was allowed to stand at room temperature for 2–2.5 hours. The dimethyl esters of *m*- and *p*-nitrobenzoyl- and 3,5-dinitrobenzoylamidophosphoric acids crystallized out almost completely under these conditions. The dimethyl esters of benzoyl-, *p*-chlorobenzoyl-, and trichloroacetylamidophosphoric acids remained in solution. In these cases the methanol was almost completely removed by vacuum distillation, and the crystalline precipitate was filtered by suction, washed with water, and air-dried. The yields indicated in the table are without utilization of the mother liquor. Such utilization gave almost quantitative yields.

Diaryl Esters of Acylamidophosphoric Acids. The trichlorophosphazoyl (0.1 mole) was dissolved in dioxane (40 ml); the solution was cooled with ice water and stirred while adding a mixture of phenol (0.3 mole) and pyridine (0.32 mole) at such a rate that the temperature of the reaction mixture did not exceed 15° (10–15 minutes). Then mixing was continued at room temperature for 2 hours, 100–150 ml of ice water was added, and stirring was continued 2 hours more. The precipitated diesters were filtered off by suction, washed with water (3×25 ml), and air-dried.

Triethylamine or dimethylaniline may be used in place of pyridine. The reaction was also carried out under the conditions described above, using 0.1 mole of the trichlorophosphazoyls with 0.2 mole of the phenols and 0.2 mole of pyridine.

Trichlorophosphazo-*p*-methoxybenzoyl (*p*-CH₃OC₆H₄CON=PCl₃) was obtained by the usual method [8]. Yields quantitative. Readily soluble in benzene, acetone, or dioxane—difficultly soluble in ether, petroleum ether, or carbon tetrachloride. Almost colorless liquid.

Found: Equiv. after hydrolysis 4.97. C₈H₇O₂NPCl₃.

Calculated: Equiv. after hydrolysis 5.00.

SUMMARY

A preparative method has been developed for obtaining dimethyl esters and diaryl esters of acylamidophosphoric acids directly from trichlorophosphazoyls and methyl alcohol or from trichlorophosphazoyls and phenols in the presence of tertiary bases.

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POLYMERIZATION OF N-DIAROXYPHOSPHINYLARENEAMIDINES

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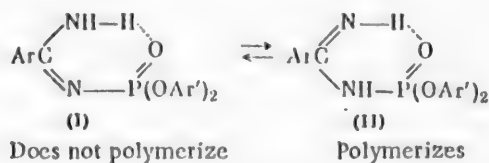
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In previous work [1] it was shown that the interaction of acid chlorides of N-diaroxyphosphinylareneimino-carboxylic acids with ammonia gives N-diaroxyphosphinylareneamides $\text{ArC}(=\text{NPO}(\text{OAr}')_2)\text{NH}_2$. By the action of strong mineral acids on N-diaroxyphosphinylareneamides they are polymerized rapidly and quantitatively, forming colorless crystalline substances which do not possess basic properties (see Table 1). Based on elemental composition and determination of molecular weight (Rast method), they are trimers of the N-diaroxyphosphinylareneamides. The polymerization occurs very readily in the presence of small quantities of strong mineral acids, formic acid, or acetic acid, but benzoic acid solutions do not give any change. If the hydrochlorides of the N-diaroxyphosphinylareneamides are left in air, they are quantitatively converted to trimers within a few days, but in storage without access of moisture of the air they are unchanged in the course of many months. Polymerization occurs readily upon boiling solutions of N-diaroxyphosphinylareneamide salts in 96% ethanol and upon dissolving in concentrated sulfuric acid. For preparative purposes the most convenient method is carrying out the polymerization in aqueous alcohol or aqueous dioxane solutions in the presence of small quantities of hydrogen chloride.

The trimers of N-diaroxyphosphinylareneamides differ sharply in their properties from the original monomers: They do not possess basic properties; they are considerably higher-melting and are almost insoluble in the majority of organic solvents, including those in which the monomers are readily soluble; they are unchanged by the action of dilute solutions of acids or alkalis at 20° or by boiling for a short time.

The cause of polymerization is usually unsaturation of the molecule. Hence, in the N-diaroxyphosphinylareneamide molecules there must be an active double bond which causes their trimerization. It is evident that the double bond in the N-diaroxyphosphinylareneamides can be only between the carbon atom and one of the nitrogen atoms, corresponding to the two possible tautomeric forms.



The double bond $>\text{C}=\text{N}^1$ cannot be the cause of polymerization, since substances whose molecules contain a bond of this type, for example $\text{ArC}(=\text{NPO}(\text{OR})_2)\text{OR}'$ [2], $\text{ArC}(=\text{NPO}(\text{OR})_2)\text{Cl}$ [3], and others, do not tend to polymerize, which probably is explained by the considerable polarization of the $>\text{C}=\text{N}^1$ bond.

*The N^1 denotes a nitrogen atom which is connected with a phosphinyl or sulfonyl.

TABLE 1

Trimers of N-Diaroxyposphorylareneamides, of the Type $\{ArC[=NPO(OAr')_2]NH_2\}_3$

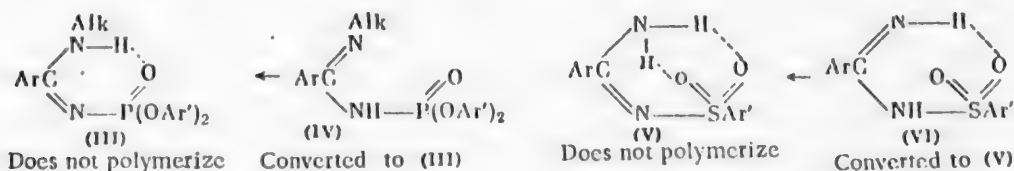
Ar	Ar'	Yield, %	Melting point	Appearance	Found (%)	Empirical formula	Calculated (%)
C_6H_5	C_6H_5	75	198–200°	Prisms (from alcohol)	N 7.63, 7.55; P 8.57, 8.90 M 1107, 1050***	$C_{57}H_{51}O_9N_3P_3$ **	N 7.95; P 8.31 M 1056
C_6H_5	p-ClC ₆ H ₄	92	191–193	Prisms (from alcohol)	N 6.24, 6.45; M 1270, 1380***	$C_{57}H_{45}O_9N_3P_3Cl_3$ *	N 6.64 M 1263
p-ClC ₆ H ₄	C_6H_5	89	215–217	Prisms (from alcohol)	Cl 8.93, 8.96	$C_{57}H_{49}O_9N_3P_3Cl_3$ *	Cl 9.16
p-ClC ₆ H ₄	p-ClC ₆ H ₄	89	202–203	Prisms (from alcohol)	N 6.01, 5.88	$C_{57}H_{43}O_9N_3P_3Cl_3$ *	N 6.14
m-NO ₂ C ₆ H ₄	C_6H_5	91	198–200	Prisms (from alcohol)	N 10.66, 10.60	$C_{57}H_{43}O_{15}N_9P_3$ **	N 10.57
m-NO ₂ C ₆ H ₄	p-ClC ₆ H ₄	93	200–201	Prisms (from dioxane)	Cl 15.45, 15.25	$C_{57}H_{42}O_{15}N_9P_3Cl_3$ **	Cl 15.21
p-NO ₂ C ₆ H ₄	C_6H_5	100	242–244	Prisms (from dioxane)	N 10.77, 10.73 M 1220, 1191***	$C_{57}H_{45}O_{15}N_9P_3$ **	N 10.57 M 1191
p-NO ₂ C ₆ H ₄	p-ClC ₆ H ₄	87	215–217	Prisms (from dioxane)	Cl 14.95, 15.01	$C_{57}H_{42}O_{15}N_9P_3Cl_3$ **	Cl 15.21
3,5-(NO ₂) ₂ C ₆ H ₃	C_6H_5	90	258–260	Prisms (from dioxane)	N 12.76, 12.87	$C_{57}H_{45}O_{21}N_{13}P_3$ **	N 12.67
3,5-(NO ₂) ₂ C ₆ H ₃	p-ClC ₆ H ₄	87	228–230	Prisms (from dioxane)	Cl 13.87, 13.67	$C_{57}H_{39}O_{21}N_{13}P_3Cl_3$ **	Cl 13.57

* Low solubility in alcohol or dioxane, still less in benzene, ether, or acetone; insoluble in carbon tetrachloride or petroleum ether.

** Low solubility in dioxane; almost insoluble in ether, benzene, petroleum ether, alcohol, carbon tetrachloride, or acetone.

*** By Rast method, in camphor.

The double bond $>C=N^2$ may be the cause of polymerization, since substances whose molecules contain an analogous grouping, for example anhydroformaldehydeaniline [4], iminoaldehydes [5], and others, are polymerized readily. If this reasoning is correct, then N^2 -monoalkylated N^1 -diaroxyphosphinylareneamidines and N -arylsulfonylareneamidines should not polymerize, since for these compounds the tautomeric forms (IV) and (VI) which contain the $>C=N^2$ double bond are not possible, as the oxygen atoms (at the phosphorus and sulfur respectively) must "draw off" the hydrogen atoms, converting them to the tautomeric forms (III) and (V), which contain $>C=N^1$ double bonds.



Experiments confirmed these assumptions. Actually, neither the N^2 -monoethyl- N^1 -diaroxyphosphinylareneamidine nor the N -aroxysulfonylareneamidine polymerizes even under the action of concentrated mineral acids. Thus, it is extremely probable that the cause of polymerization of N -diaroxyphosphinylareneamidines in the presence of the $>C=N^2$ double bond is occasioned by the characteristics of the structure of the amidine grouping as a whole, namely the presence at the N^1 of a strongly electronegative substituent with only one atom of oxygen capable of forming a hydrogen bond, and the presence of two hydrogen atoms at the N^2 .

For the present work, several N -diaroxyphosphinylareneamidines were obtained which have not been described in the literature (Table 2); the method of preparation was found previously [1].

EXPERIMENTAL

Polymerization of N -Diaroxyphosphinylbenzamidines, N -Diaroxyphosphinyl-*p*-chloro- and -nitrobenzamidines. To a solution of 0.01 mole of the N -diaroxyphosphinylbenzamide in 10 ml of ethanol there was added 3-4 ml of 0.5 N hydrochloric acid; the mixture was heated to boiling and then allowed to stand for a day at room temperature. The precipitated crystals of the trimers were filtered off by suction, washed with alcohol (2x3 ml), washed with ether (2x2 ml), and air-dried.

Polymerization of N -Diaroxyphosphinyl-nitrobenzamidines was carried out in aqueous dioxane solutions, since they were difficultly soluble in ethanol.

The trimers of all N -diaroxyphosphinylbenzamidines were recrystallized from dioxane or alcohol-dioxane mixture. Yields and melting points - see Table 1.

Polymerization of N -Diaroxyphosphinylbenzamidines in the Presence of Formic or Acetic Acid. An 0.01 mole quantity of the N -diaroxyphosphinylbenzamide was dissolved with heating in 10 ml of 80% ethanol, 3 ml of acetic or formic acid was added, and the mixture was boiled 1-2 minutes and allowed to stand for a day. Further treatment was as in the preceding section. Trimer yields 80-90%. The N -diaroxyphosphinylbenzamidines were not changed upon boiling with aqueous alcohol solutions or benzoic or *p*-chlorobenzoic acids.

Polymerization of N -Diphenoxyphosphinylbenzamide by the Action of Concentrated Sulfuric Acid. An 0.006 mole quantity of N -diphenoxyphosphinylbenzamide was dissolved with vigorous mixing in 2 ml of sulfuric acid (d 1.84). The temperature rose to 45-50°. The transparent solution was diluted by rapid addition of 15 ml of water. After 3 hours the precipitated trimer was filtered off by suction, washed, and recrystallized. Yield 90%.

Trimer of N -Diphenoxyphosphinylbenzamide from Its Hydrochloride. a) Upon Standing in Air. An 0.003 mole quantity of the hydrochloride of N -diphenoxyphosphinylbenzamide was placed on a tared watch glass in a dust-protected location and occasionally stirred with a glass rod. In 48 hours the glassy salt was converted to a viscous liquid, and its weight had increased due to the absorption of moisture from the air. In 72 hours trimer crystals began to precipitate, and the weight began to decrease due to evaporation of water and volatilization of hydrogen chloride. In 5 days all of the liquid was converted to a dry, crystalline mass, and its weight corresponded exactly to 0.001 mole of the trimer of N -diphenoxyphosphinylbenzamide. The trimer was washed with alcohol and ether and dried. Identification - by means of mixed-sample test.

TABLE 2

N-Di-p,p'-chlorodiphenoxyphosphinylareneamidines of the Type $\text{ArC}[\text{NPO}(\text{C}_6\text{H}_4\text{Cl-p})_2]\text{NH}_2$ *

Ar	Yield, %	Melting point	Appearance	Found (%)	Empirical formula	Calculated (%)
C_6H_5	75	122–124°	Needles (from 80% alcohol)	N 6.71, 6.78	$\text{C}_{19}\text{H}_{15}\text{O}_3\text{N}_3\text{P}_2\text{Cl}_2$	N 6.64
p- ClC_6H_4	97	132–134	Interlocked needles (from alcohol)	Cl 23.91, 23.83	$\text{C}_{19}\text{H}_{14}\text{O}_3\text{N}_3\text{P}_2\text{Cl}_3$	Cl 23.35
p- $\text{NO}_2\text{C}_6\text{H}_4$	81	148–150	Prisms (from alcohol)	Cl 15.80, 15.63	$\text{C}_{19}\text{H}_{13}\text{O}_3\text{N}_3\text{P}_2\text{Cl}_2$	Cl 15.21
m- $\text{NO}_2\text{C}_6\text{H}_4$	88	149–151	Interlocked needles (from alcohol)	Cl 14.97, 14.90	$\text{C}_{19}\text{H}_{13}\text{O}_3\text{N}_3\text{P}_2\text{Cl}_2$	Cl 15.21
3,5-(NO_2) $_2\text{C}_6\text{H}_3$	100	208–210	Prisms (from alcohol)	Cl 13.59, 13.74	$\text{C}_{19}\text{H}_{13}\text{O}_7\text{N}_4\text{P}_2\text{Cl}_3$	Cl 13.87

* All substances were rather readily soluble in dioxane or acetone, difficultly soluble in benzene or alcohol, very difficultly soluble in petroleum ether, carbon tetrachloride, or ether.

b) Upon Boiling with 96% Ethanol. A solution of 0.001 mole of the hydrochloride of N-diphenoxyphosphinylbenzamidine in 25 ml of alcohol was boiled for 5–6 minutes and allowed to stand. After a day the precipitated trimer was filtered off by suction, washed with alcohol and ether, and dried. Yield 80%.

N-Ethyl-N'-diphenoxyphosphinylbenzamidine. To a solution of 0.03 mole of N-diphenoxyphosphinyliminobenzoyl chloride in 70 ml of 1 : 1 acetone-ether mixture, cooled to -15°, 0.06 mole of ethylamine (also cooled to -15°) was added with stirring, and the mixture was allowed to stand for a day at 0°. The solvents were removed by vacuum distillation. The colorless crystalline mass in the residue was washed with water (2 x 5 ml), alcohol (2 x 2 ml), ether (2 x 2 ml), and dried. Yield almost quantitative. Prisms; m. p. 122–123° (from alcohol). Readily soluble in acetone, difficultly soluble in alcohol, benzene, or carbon tetrachloride, insoluble in water, ether, or petroleum ether.

Found %: P 8.70. $\text{C}_{21}\text{H}_{21}\text{O}_3\text{N}_2\text{P}$. Calculated %: P 8.58.

N²,N'-Ethylene-bis-N¹-diphenoxyphosphinylbenzamidine, $\text{C}_6\text{H}_5\text{C}[\text{NPO}(\text{OC}_6\text{H}_5)_2]\text{NHCH}_2\text{CH}_2\text{NH}[(\text{C}_6\text{H}_5\text{O})_2\text{PON}=\text{CC}_6\text{H}_5]$ was obtained from N-diphenoxyphosphinyliminobenzoyl chloride and ethylenediamine under the same conditions as those for N-ethyl-N'-diphenoxyphosphinylbenzamidine. Colorless crystals, difficultly soluble in alcohol, dioxane, ether, or acetone, and still more difficultly soluble in water, benzene or petroleum ether. After recrystallization from 1 : 1 alcohol-dioxane mixture, prisms, m. p. 183–185°. Yield quantitative.

Found %: N 7.37. $\text{C}_{40}\text{H}_{36}\text{O}_6\text{N}_4\text{P}_2$. Calculated %: N 7.66.

Action of Acids on N-Ethyl-N'-diphenoxyphosphinylbenzamidine and N-Arylsulfonylareneamidines. These experiments were carried out both under the conditions used for polymerizing the N-diaroxyphosphinylareneamidines and also under other very diverse conditions. In all cases the original products were recovered.

SUMMARY

1. By the action of strong mineral acids on N-diaroxyphosphinylareneamidines, they are converted quantitatively to crystalline polymers, which do not possess basic properties. N-Diaroxyphosphinyl-N'-alkylareneamidines and N-arylsulfonylareneamidines are unchanged by the action of acids.

2. The polymerization of N-diaroxyphosphinylareneamidines apparently is caused by the presence in their molecules of an active double bond in the amidine

group between the carbon atom and the nonacylated nitrogen atom. N-Diaroxyphosphinyl-N'-alkylarene-amidines and N-arylsulfonylareneamidines do not polymerize, since the nature of their structure does not permit the formation of tautomeric forms with an active double bond in the amidine group.

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TRICHLOROPHOSPHAZO-N-ARYLSULFONYLIMINOBENZOYLS

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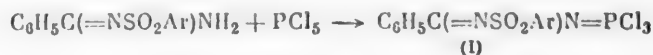
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Derivatives of amidines, substituted on the nitrogen atoms by phosphoric acid radicals possess great physiological importance [1]. Despite this, very few compounds of this type are known [2], and methods for their synthesis have only begun to be developed. As the result of the recently found phosphazo reaction [3] it has become possible to obtain highly diverse trichlorophosphazoyls of general formula $AcN=PCl_3$, where Ac can be: $ClSO_2$, $ArCO$, RSO_2 , CCl_3CO , etc. [4].

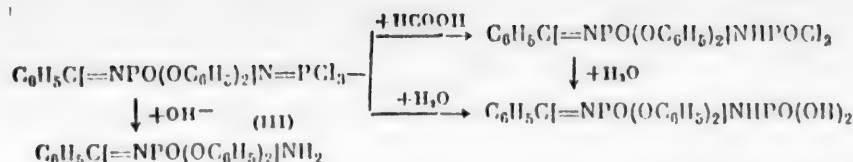
It was interesting to study the possibility of obtaining amidines, phosphorylated on the nitrogen atoms, employing the phosphazo reaction. Experiments revealed that N-arylsulfonylbenzamidines react with phosphorus pentachloride to yield trichlorophosphazo-N-arylsulfonyliminobenzoyls (I).



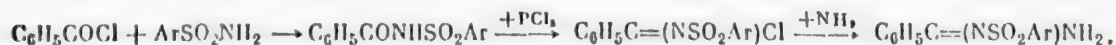
The reaction goes quantitatively in a matter of 25-35 min at 80-120° in an inert solvent. Completely pure trichlorophosphazo-N-arylsulfonyliminobenzoyls (I) (Table 1) are obtained when chemically pure starting products are used. The former are comparatively low-melting crystalline compounds (with the exception of compound 3 (Table 1), which was obtained as a viscous liquid). The compounds are readily soluble in benzene, dioxane, and acetone, and difficultly soluble in ether, petroleum ether, and carbon tetrachloride. At room temperature the compounds react slowly with water, and when refluxed with water they are cleaved into the starting N-arylsulfonylamidines, phosphoric acid and hydrogen chloride. When reacted with 1 mole of anhydrous formic acid or glacial acetic acid they give the corresponding N-dichlorophosphinyl-N'-arylsulfonylbenzamidines (II) $[C_6H_5C(=NSO_2Ar)NHPOCl_2]$ in 90-95% yield (Table 2).

The reaction begins at room temperature, goes with the evolution of heat, and is ended in 1 to 2 hours. (II) are fairly high-melting crystalline substances, melting with decomposition. With water at 20° they react slower than do compounds (I), and when boiled with water they are cleaved to the N-arylsulfonylamidines, phosphoric acid and hydrogen chloride. They are difficultly soluble in benzene, dioxane, and acetone, and are very difficultly soluble in petroleum ether, carbon tetrachloride, and ether.

Trichlorophosphazo-N-diphenoxyphosphinyliminobenzoyl (III), $\{C_6H_5C[=NPO(OC_6H_5)_2]N=PCl_3\}$, a colorless viscous liquid, distilling with decomposition, is obtained in quantitative yield when N-diphenoxyphosphinylbenzamide is reacted with phosphorus pentachloride. In its chemical properties the compound differs from the (I) compounds. When (III) is refluxed with water the product formed is N-diphenoxyphosphinylbenzamide-N'-phosphoric acid, and not N-diphenoxyphosphinylbenzamide. The same acid is also obtained when N-dichlorophosphinyl-N'-diphenoxyphosphinylbenzamide, which is formed in the formolysis of (III), is hydrolyzed with water in acetone solution. The starting N-diphenoxyphosphinylbenzamide is obtained when (III) is refluxed with 0.1 N sodium hydroxide solution.



To synthesize compounds 3, 4 and 6 (Table 1) we first prepared the previously unknown N-arylsulfonylbenzamidine in accordance with the scheme.



The N-benzoylarenesulfonamides were obtained by the O. Wallach method [5], the N-arylsulfonyliminobenzoyl chlorides by the A. Wolkoff method [6], and the N-arylsulfonylbenzamidines by our earlier described method [7] (see Table 3).

EXPERIMENTAL

All of the operations were carried out in such manner that both the reaction mixtures and the reaction products were protected from atmospheric moisture as much as possible.

Trichlorophosphazo-N-arylsulfonyliminobenzoyls (I) (Table 1). A mixture of 0.15 mole of N-arylsulfonylbenzamidine, 60 ml of benzene or toluene, and 0.155 mole of pulverized phosphorus pentachloride was placed in a round-bottomed flask, fitted with a reflux condenser, and heated in an oil bath at 80–120° until the hydrogen chloride ceased to evolve, which required 30–40 min. During this time 95–100% of the theoretical amount of hydrogen chloride was evolved, which was trapped and determined in conventional manner. The solvent was vacuum-distilled. The residue was an oil, which crystallized when allowed to stand with 10 ml of petroleum ether for 2–3 days and occasional rubbing with a glass rod. The crystals were suction-filtered, washed with petroleum ether (2×5 ml), and dried. If necessary, (I) can be recrystallized from either benzene or a mixture of benzene and petroleum ether (1 : 1). The melting points of the recrystallized products were usually the same as the melting points of the crude products. Only in some cases did the melting points after recrystallization increase by 1–1.5°.

Formolysis and acetolysis of trichlorophosphazo-N-arylsulfonyliminobenzoyls. Anhydrous formic acid (0.01 mole) was added slowly, in drops, to a solution of 0.01 mole of (I) in 30–40 ml of dry benzene (if necessary, warmed slightly). Stormy reaction began immediately, accompanied by self-heating of the mixture (–75°) and the evolution of carbon monoxide and hydrogen chloride. Soon the N-dichlorophosphinyl-N'-arylsulfonylbenzamidine (II) began to deposit from the solution. The reaction mixture was allowed to stand for 1–2 hr, and the deposited crystals were suction-filtered, washed with benzene (2×5 ml), and dried. The obtained products were quite pure and did not require recrystallization (see Table 2).

The acetolysis experiments were run under the same conditions, but here 1.5 moles of anhydrous acetic acid per mole of (I) was used. The yields were nearly quantitative.

Hydrolysis of trichlorophosphazo-N-arylsulfonyliminobenzoyls with water. A mixture of 0.001 mole of (I) and 50 ml of water was refluxed for 30–40 min. Then the mixture was cooled, and the obtained crystalline N-arylsulfonylbenzamidines were suction-filtered, washed with water (2×3 ml), then with alcohol (1×3 ml), and dried. The yields were nearly quantitative. The compounds were identified by the technique of mixed melting points.

Trichlorophosphazo-N-diphenoxyphosphinyliminobenzoyl (III) was obtained in the same manner as (I). The yield was nearly quantitative; the compound was a viscous colorless liquid.

Found %: Cl 22.30, 22.07; equiv. after hydrolysis 5.00, 5.01. $\text{C}_{19}\text{H}_{15}\text{O}_3\text{N}_2\text{P}_2\text{Cl}_3$. Calculated %: Cl 21.82; equiv. after hydrolysis 5.00.

N-Dichlorophosphinyl-N'-diphenoxyphosphinylbenzamidine (IV) was obtained by the formolysis of (III), in the same manner as the (I) compounds were obtained from (II). Yield 86%; colorless prisms, m. p. 159–161° (from benzene); difficultly soluble at 20° in the common organic solvents. The compound is slowly hydrolyzed by water at 20°, and rapidly when heated at the boil.

TABLE 1

Trichlorophosphazo-N-arylsulfonyliminobenzoyls of Type $C_6H_5C(=NSO_2Ar)N=PCl_3$

Ar	Yield (in %)	Melting point	Appearance	Found		Calculated [*] (%)
				%	equiv. after hydroly.	
C_6H_5	100	59—61°	Prisms (from a mixture of benzene and petroleum ether)	Cl 26.38, 26.12; P 7.91, 8.07	4.85, 5.10	Cl 26.89; P 7.83
p- $ClH_3C_6H_4$	100	81—83	Prisms (from a mixture of benzene and petroleum ether)	Cl 25.40, 25.45	5.00, 5.00	Cl 25.98
p- ClC_6H_4	84	Liquid	Prisms (from benzene)	Cl 24.80, 25.00**	4.78, 4.90	Cl 24.75**
p- $NO_2C_6H_4$	91	143—145	Prisms (from benzene)	Cl 24.10, 24.31; N 9.31, 9.27	5.01, 5.02	Cl 24.14; N 9.53
m- $C_{10}H_7$	96	124—125	Prisms (from benzene)	Cl 21.94, 22.14; P 7.13, 7.16	4.89, 4.96	Cl 23.80; P 6.94
p- $C_{10}H_7$	100	97—100	Prisms (from benzene)	Cl 23.11, 23.92	4.93, 4.94	Cl 23.86

TABLE 2

N-Dichlorophosphinyl-N'-arylsulfonylbenzamidines (II) of Type $C_6H_5C(=NSO_2Ar)NHPOCl_2$

Ar	Yield (in %)	Melting point	Found		Empirical formula	Calculated ^{****} (%)
			%	equivalents after hydrolysis		
C_6H_5	92	123—125°	Cl 18.20, 18.01	3.89, 3.91	$C_{13}H_{11}O_3N_2SPCl_2$	Cl 18.80
p- $ClH_3C_6H_4$	96	174—176	Cl 18.80, 18.75; P 7.87, 7.83		$C_{14}H_{13}O_3N_2SPCl_2$	Cl 18.12; P 7.92
p- ClC_6H_4	96	166—167	Cl 26.12, 26.32;****	3.98, 3.91	$C_{13}H_{10}O_3N_2SPCl_3$	Cl 25.85; N 6.80
p- $NO_2C_6H_4$	98	183—184	Cl 16.17, 16.18	3.98, 3.91	$C_{13}H_{10}O_3N_2SPCl_2$	Cl 16.75
m- $C_{10}H_7$	94	177—178	Cl 16.61, 16.86	3.96, 4.00	$C_{17}H_{13}O_3N_2SPCl_2$	Cl 16.60
p- $C_{10}H_7$	100	162—163	Cl 16.38, 16.08; N 6.92, 6.91	3.95, 3.96	$C_{17}H_{13}O_3N_2SPCl_3$	Cl 16.60; N 6.55

* Calculated equiv. after hydrolysis = 5.00.

** Hydrolyzable chlorine.

*** All of the compounds crystallize from benzene as prisms.

**** Calculated: equiv. after hydrolysis = 4.00.

***** Hydrolyzable chlorine.

TABLE 3

Ar	Yield (in %)	Melting point	Appearance	Found		Empirical formula	Calculated		Solubility*				
				%	equiv. after hydroly.		%	equiv. after hydroly.	alcohol	ether	acetone	petroleum ether	CCl ₄
N-Benzoylarenosulfonamides of Type C ₆ H ₅ CONHSO ₂ Ar													
p-NO ₂ C ₆ H ₄	96	196—199°	Prisms (from alcohol)	N 9.18, 9.13	1.01	C ₁₃ H ₁₀ O ₃ N ₂ S	N 9.14	1.00	+	=	+++	=	=
p-C ₁₀ H ₇	98	188—190	Prisms (from alcohol)	—	1.00	C ₁₇ H ₁₃ O ₃ NS	—	1.00	+	=	+++	=	=
N-Arylsulfonyliminobenzoyl Chlorides of Type C ₆ H ₅ C(=SO ₂ Ar)Cl													
p-ClC ₆ H ₄	100	105—107	Prisms (from a mix - ture of benzene and petroleum ether)	Cl 11.40, 11.26**	1.98	C ₁₃ H ₉ O ₂ NSCl ₂	Cl 11.29	2.00 (de- comp.)	+	=	++	=	—
p-NO ₂ C ₆ H ₄	84	155—157	Prisms (from benzene)	Cl 10.76, 10.48	2.01	C ₁₃ H ₉ O ₄ N ₂ SCl	Cl 10.42	2.00 (de- comp.)	=	=	+++	=	—
p-C ₁₀ H ₇	100	93—94	Prisms (from benzene)	Cl 11.06, 11.12	1.93	C ₁₇ H ₁₂ O ₂ NSCl	Cl 10.73	2.00 (de- comp.)	=	=	+++	=	—
N-Arylsulfonylbenzamidines of Type C ₆ H ₅ C(=NSO ₂ Ar)NH ₂													
C ₆ H ₅	99	149—151***	Prisms (from alcohol)	N 10.60, 10.66	—	C ₁₃ H ₁₃ O ₃ N ₂ S	N 10.76	—	+	+	+++	=	—
p-ClC ₆ H ₄	75	107—108	Prisms (from alcohol)	N 9.68, 9.87	—	C ₁₃ H ₁₁ O ₂ N ₂ SCl	N 9.50	—	—	+	+++	=	—
p-NO ₂ C ₆ H ₄	100	175—177	Prisms (from methanol)	N 13.59, 13.60	—	C ₁₃ H ₁₁ O ₄ N ₂ S	N 13.76	—	—	=	+++	=	=
p-C ₁₀ H ₇	66	159—161	Prisms (from a mixture of acetone and al- cohol)	N 9.06, 8.97	—	C ₁₇ H ₁₄ O ₂ N ₂ S	N 9.03	—	—	—	+++	=	=

* Legend: † readily soluble at 20°; + readily soluble at the boiling point; - difficultly soluble at the boiling point; = insoluble at the boiling point.

** Hydrolyzable chlorine.

*** According to the literature 139° [6], which is incorrect.

Found %: Cl 15.31, 15.02; P 13.09, 13.21; equiv. after hydrolysis 3.84, 3.93. $C_{21}H_{16}O_4N_2P_2Cl_2$. Calculated %: Cl 15.11; P 13.21; equiv. after hydrolysis 4.00.

N-Diphenoxyphosphinylbenzamidine-N'-phosphoric acid (V) was obtained by the hydrolysis of (IV) with water in acetone solution [8]. Yield 95%; prisms, m. p. 175–178° (from alcohol); difficultly soluble in water, alcohol, and acetone, and insoluble in petroleum ether, carbon tetrachloride, and benzene. A saturated water solution has a pH of about 4.

Found %: P 6.27; equiv. 2.01. $C_{15}H_{13}O_6N_2P_2$. Calculated %: P 6.48; equiv. 2.00.

(V) is also obtained by refluxing (III) with water for 20–30 min. Yield 80%.

Hydrolysis of N-trichlorophosphazo-N'-diphenoxyphosphinyliminobenzoyl with 0.1 N NaOH solution. A mixture of 0.01 mole of (III) and 50 ml of 0.1 N NaOH solution was refluxed for 30–40 min and then allowed to stand for 2–3 hr. The obtained crystals of N-diphenoxyphosphinylbenzamidine were suction-filtered, washed with water, and dried. Yield 85%; m. p. 101–102° (from alcohol). The compound was identified by mixed melting point.

N-Arylsulfonylbenzamidines. A slow stream of dry ammonia was passed for 3–4 hr through a solution of 0.1 mole of N-arylsulfonyliminobenzoyl chloride in 100 ml of either carbon tetrachloride or benzene. Then the reaction flask was stoppered and allowed to stand for 2–3 hr. The solvent was vacuum-distilled. The residue was a completely crystalline mass, which was pulverized, washed with water (3×5 ml) and alcohol (2×3 ml), and recrystallized from alcohol (see Table 3).

SUMMARY

1. The phosphazo reaction is applicable not only to acid amides, but also to acylated amidines. The reaction of phosphorus pentachloride with N-arylsulfonylbenzamidines yields trichlorophosphazo-N-arylsulfonyliminobenzoyls, which possess chemical properties close to those of the trichlorophosphazoacetyls.

2. The reaction of N-diphenoxyphosphinylbenzamidine with phosphorus pentachloride yields trichlorophosphazo-N-diphenoxyphosphinyliminobenzoyl, which on formolysis is converted to N-dichlorophosphinyl-N'-diphenoxyphosphinylbenzamidine, and on hydrolysis gives N-diphenoxyphosphinylbenzamidine-N'-phosphoric acid, which is relatively stable toward further hydrolysis.

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*Original Russian pagination. See C. B. translation.

DERIVATIVES OF 3-AMINOPHENOL

I. N-ARYLSULFONYL AND N-BENZOYL DERIVATIVES

OF 3-AMINOPHENOL AND ITS HOMOLOGS

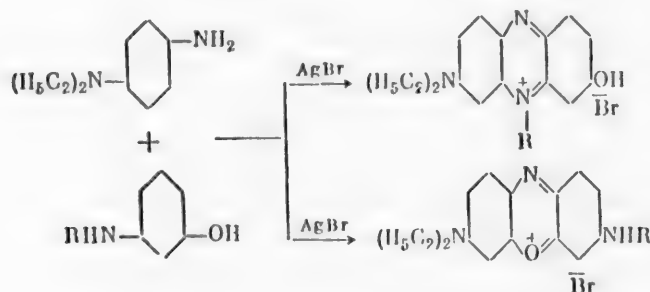
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Derivatives of 3-aminophenol under the conditions of their oxidative condensation with a p-dialkylamino-aniline, for example, in the color development reaction [1], form quinone imines that are either azine or oxazine dyes.



In a search for color development components that could be of interest in color cinematography, we synthesized 3-amino-5-hydroxy-1,2-xylene (I), 5-amino-3-hydroxy-1,2-xylene (II), 2-amino-6-hydroxy-1,4-xylene (III), 2-amino-4-hydroxytoluene (IV), 3-amino-5-hydroxytoluene (V) and 4-amino-2-hydroxytoluene (VI), and their N-benzoyl and N-sulfonyl derivatives.

(I), (III) and (V) were synthesized by a common procedure, consisting in the preparation of the dinitro compound [2, 3], partial reduction of one of the nitro groups in the latter using sodium sulfide [4], replacement of the amino group by the hydroxyl group through the diazo compound [5], and reduction of the second nitro group with hydrazine hydrate [6]. Compound (II) was obtained by the nitration of o-xylene to 3-nitro-1,2-xylene [7], reduction of the latter with hydrazine hydrate, nitration of the formed 3-amino-1,2-xylene [8], and then proceeding as indicated above. The starting materials for compounds (IV) and (VI) were 4- or 2-nitro-2- or 4-aminotoluene. To obtain the acyl derivatives of (I-VI), and also of m-aminophenol (VII), the latter were acylated with benzoyl chloride in benzene medium [9], and with benzene- and p-toluenesulfonyl chloride in aqueous medium in the presence of sodium acetate [10]. In order to isolate 2,6-dinitro-1,4-xylene from the mixture of nitro products we partially reduced the latter with hydrogen sulfide in ammoniacal methanol medium, and here the predominant product was the nitroamine from 2,3-dinitro-1,4-xylene, which proved to be readily soluble in the methanol, and consequently could be easily separated from the 2,6-dinitro-1,4-xylene.

It was established that the synthesized *m*-aminophenol derivatives do not fluoresce in ultraviolet light. The data on the color photographic properties of the obtained compounds will be reported separately.

EXPERIMENTAL

2-Nitro-4-aminotoluene, 3,5-dinitrotoluene and 3,5-dinitro-1,2-xylene were synthesized by earlier described procedures [3].

2,6-Dinitro-1,4-xylene. For the nitration we took 477 g of mixed acid (33% HNO_3 , 67% H_2SO_4) and added it in 1 hr to 106 g of 1,4-xylene at 15–20°, after which the mixture was stirred at 25° for 2 hr, and then poured into 500 g of water and ice. The precipitate was filtered, washed with 100 ml of water, and dried at 70–75°. The yield of mixed nitro products was 82 g (92.8%); m. p. 83–86°.

For purification we took 40 g of the product and dissolved it in a mixture of 250 ml of methanol and 40 ml of 23% ammonia, after which the solution was heated to the boil and then sufficient hydrogen sulfide passed into the solution in 1 hr to reduce 50% of the nitro compounds. The hot solution was filtered from sulfur, and then cooled to precipitate the 4,6-dinitro-1,4-xylene. If the obtained substance melted below 122–123°, it was recrystallized from methanol. Yield 8.2 g (19.03%), m. p. 122–123°; from the literature [2]: m. p. 123°.

3-Nitro-1,2-xylene. A mixture of 100 g of nitric acid (d 1.31) and 200 g of sulfuric acid monohydrate was added to 100 g of 1,2-xylene at –2 to 0°, after which the mixture was stirred for 1.5 hr and then poured into 700 g of ice and water. The product was purified by steam distillation from caustic. Yield 104 g (69.0%). Viscous yellow liquid, d_{20}^{20} 1.142; from the literature [7]: d_{15}^{15} 1.147.

3-Amino-1,2-xylene. A mixture of 45.7 g of 3-nitro-1,2-xylene and 45 g of hydrazine hydrate in 100 ml of methanol was heated to the boil and then about 4 g of 50% skeletal nickel paste was added in portions, followed by heating under reflux until the solution decolorized (about 2 hr). On completion of reduction, about another gram of 50% skeletal nickel paste was added to decompose the excess hydrazine hydrate. The nickel was filtered, while the methanol filtrate was distilled to a volume of 50 ml, and this residue was diluted with 100 ml of water to yield a colorless oil. Yield 35.7 g (97%); d_{20}^{20} 0.988. The amine was converted to the sulfate. From the literature [7]: the amine is a colorless liquid with d_{15}^{15} 0.993.

5-Nitro-3-amino-1,2-xylene. A solution of 34 g of 3-amino-1,2-xylene in 270 ml of sulfuric acid monohydrate was nitrated at –10° with a mixture of 15 ml of nitric acid (d 1.4) and 45 ml of sulfuric acid monohydrate, after which the mixture was stirred for 1 hour and then poured over 600 g of ice. Yield 13.3 g (31%). The sulfate of the nitroamine was suspended in 150 ml of water and then ammonia was added until the test with Brilliant Yellow was positive. The product was recrystallized from 150 ml of 80% methanol. Yield 4.22 g (17.9%); m. p. 110–111°; from the literature [8]: yellow needles, m. p. 111–112° (from 80% methanol).

Nitroamino derivatives of toluene and the xylenes. The dinitro compound (0.1 mole) was added to 250 ml of water, 0.27 mole of sodium sulfide was sifted in, then 0.26 mole of ammonium sulfate, and the mixture was stirred for 2 hr at 70–72° (A), or the dinitro compound (0.1 mole) was added to 120 ml of methanol, then 0.27 mole of sodium sulfide was sifted in, the whole refluxed for 40 min, and then the mixture was diluted with 150 ml of water (B). The precipitate was filtered, then suspended in a mixture of 200 ml of water and 20 ml of hydrochloric acid (d 1.19), the whole stirred for 10 min at 60°, and the solution was then filtered. The nitroamino compounds were precipitated by the addition of ammonia, and then recrystallized from either aqueous methanol or water (Table 1).

Nitrohydroxy derivatives of toluene and the xylenes. The nitroamino compound (0.1 mole) was sifted into a mixture of 120 ml of water and 30 ml of concd. sulfuric acid, and then a solution of 0.102 mole of sodium nitrite in 30 ml of water was added at 0–2° until a distinct test with starch-iodide paper was obtained, after which the reaction mass was stirred for another 0.5 hr. The diazonium salt solution was added to a boiling mixture of 100 ml of water and 130 ml of concd. sulfuric acid, and the whole was refluxed for 15 min. The nitrohydroxy compounds were recrystallized from water and were obtained as yellow needles (Table 2).

Aminohydroxy derivatives of toluene and the xylenes. A mixture of 0.01 mole of the *m*-nitrohydroxy compound and 0.032 mole of hydrazine hydrate was dissolved in 20 ml of methanol, the solution heated to the boil, and then about 2 g of 50% skeletal nickel paste was added in portions.

TABLE 1

Nitroamino Derivatives of Toluene and Xylenes

Expt. No.	Name of compound	Method	Yield (in %)	Appearance	Melting point
1	3-Nitro-5-amino-1,2-xylene	B	50.0	Orange plates	74-75° (from 60% methanol) (74-75° [8])
2	2-Nitro-6-amino-1,4-xylene	B	33.4	Yellow needles	96-97° (from 50% methanol) (96° [4])
3	3-Nitro-5-aminotoluene	A	14.4	Red needles	97-98° (from water) (98-98.4° [11])

TABLE 2

Nitrohydroxy Derivatives of Toluene and Xylenes

Expt. No.	Name of compound	Yield (in %)	Melting point (from water)
1	3-Nitro-5-hydroxy-1,2-xylene	21.0	111-112°
2	5-Nitro-3-hydroxy-1,2-xylene	42.4	120-121, 109 [12]
3	2-Nitro-6-hydroxy-1,4-xylene	35.2	90-91, 91 [5]
4	2-Nitro-4-hydroxytoluene	35.8	76-79, 77.0-77.4 [11]
5	3-Nitro-5-hydroxytoluene	21.4	61-62, 60-62 [11]
6	4-Nitro-2-hydroxytoluene	40.1	117-118, 106-108 [13]

TABLE 3

Aminohydroxy Derivatives of Toluene and Xylenes

Expt. No.	No. of synthesized compound	Yield (in %)	Melting point	Appearance	% N		
					Found	Empirical formula	Calculated
1	I	65.1	210-211° (from 60% methanol)	Colorless prisms	10.21, 10.39	C ₈ H ₁₁ ON	10.20
2	II	79.6	179-180 (from 50% methanol) (179° [12])	Likewise	-	-	-
3	III	36.2	153-154 (from water)	Colorless plates	10.22, 10.08	C ₈ H ₁₁ ON	10.20
4	IV	51.0	156-157 (from 50% methanol) 157-159 [14]	Likewise	-	-	-
5	V	52.0	137-138 (from 50% methanol)	Colorless prisms	11.19, 11.27	C ₇ H ₉ ON	11.38
6	VI	61.7	161-162 (from water) (159-161° [13])	Colorless plates	-	-	-

After the yellow color of the solution had disappeared, the excess hydrazine hydrate was decomposed by the addition of 0.1 g of 50% skeletal nickel paste, and then the stirring under reflux was continued until the test with Brilliant Yellow was negative (about 15 min). The nickel was filtered, and the filtrate was diluted with 30 ml of water to precipitate the reaction product. The obtained aminohydroxy derivatives (I-VI) were recrystallized from aqueous methanol (Table 3).

•Found %: N 8.65, 8.46. C₈H₉O₃N. Calculated %: N 8.37.

TABLE 4

N-Arylsulfonyl Derivatives of (I-VII)

Synthesized compounds ^a	Yield (in %)	Melting point	Appearance	Found (%)				Empirical formula	Calculated (%)			
				C	H	N	S		C	H	N	S
1 N-R-I	66.8	152-153° (from 35% methanol)	Colorless prisms	60.27, 60.03	5.62, 5.43	4.78, 4.76	11.15, 11.05	C ₁₄ H ₁₃ O ₃ NS	60.60	5.42	5.06	11.55
2 N-R-II	65.0	180.5-181° (from 50% methanol)	Colorless crystals	60.55, 60.35	5.38, 5.45	4.70, 4.68	11.45, 11.49		60.60	5.42	5.06	11.55
3 N-R-III	53.5	203.5-204° (from 50% methanol)	Likewise	—	—	5.23, 5.16	11.64, 11.79		60.60	5.42	5.06	11.55
4 N-R-IV	84.0	183-184° (from 50% methanol), (183° [15])	• •	—	—	—	—	C ₁₃ H ₁₃ O ₃ NS	—	—	—	—
5 N-R-V	53.2	88-89° (from 25% methanol)	Colorless prisms	—	—	5.37, 5.18	12.19, 12.31		—	—	5.32	12.15
6 N-R-VI	40.1	130-131° (from water)	Likewise	59.32, 59.40	5.25, 5.27	5.27, 5.20	12.02, 11.97		59.40	4.95	5.32	12.15
7 N-R-VII	49.2	129-130° (from water)	Colorless needles	57.67, 57.97	4.46, 4.36	5.69, 5.69	12.45, 12.34	C ₁₂ H ₁₁ O ₃ NS	57.85	4.42	5.63	12.72
8 N-R'-VI	26.2	132-133° (from water)	Colorless prisms	60.49, 60.05	5.36, 5.42	4.99, 4.93	—	C ₁₄ H ₁₃ O ₃ NS	60.60	5.42	5.06	—
9 N-R'-VII	23.7	156-157° (from water) [16]	Colorless needles	—	—	—	—	—	—	—	—	—



TABLE 5

N-Benzoyl Derivatives of (I-IV) and (VI-VII)

Expt. No.	Synthesized compounds	Yield (in %)	Melting point	Appearance	Found (%)			Empirical formula	Calculated (%)		
					C	H	N		C	H	N
1	N-R - I	39.5	205-206° (from 60% methanol)	Colorless prisms	75.06, 74.84	6.59, 6.47	5.73, 5.67	$C_{15}H_{15}O_2N$	74.7	6.23	5.81
2	N-R - II	49.9	158-159° (from 50% methanol)	Colorless needles	74.11, 74.30	6.08, 6.20	6.00, 5.82		74.7	6.23	5.81
3	N-R - III	47.8	187-188° (from 30% methanol)	Likewise	74.37, 74.36	6.19, 6.20	5.64, 5.92		74.7	6.23	5.81
4	N-R - IV	39.4	163-164° (from 50% methanol)	Colorless prisms	74.22, 74.47	6.23, 6.07	6.28, 6.14	$C_{14}H_{13}O_2N$	74.2	5.77	6.15
5	N-R - VI	39.6	201-202° (from 50% methanol)	Likewise	74.40, 74.42	5.96, 5.72	6.08, 6.05		74.2	5.77	6.15
6	N-R - VII	40.5	169-170° (from water) (171° [17])	Colorless needles	—	—	—	—	—	—	—



N-Arylsulfonyl derivatives of (I-VII). A suspension of 0.01 mole of (I-VII), 0.011 mole of either benzene- or p-toluenesulfonyl chloride, and 0.011 mole of sodium acetate in 80 ml of water was refluxed for 6 hr, then cooled to 20°, after which the precipitate was filtered and washed with water (about 20 ml). The N-arylsulfonyl derivatives were recrystallized from either aqueous methanol or water (Table 4).

N-Benzoyl derivatives of (I-IV) and (VI-VII). A mixture of 0.01 mole of (I-IV) or (VI-VII) and 0.01 mole of benzoyl chloride in 50 ml of dry benzene was refluxed for 10 hr, then cooled to 20°, and the product filtered and washed with benzene (about 20 ml). The benzoyl derivatives were recrystallized from either aqueous methanol or water (Table 5).

SUMMARY

A number of N-arylsulfonyl and N-benzoyl derivatives of 3-aminophenol and its homologs was synthesized. Some of the properties of the synthesized compounds were investigated.

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ACTION OF NITROGEN TETROXIDE ON CROTONIC ACID

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The action of nitrogen tetroxide on ethylene and pseudobutylene gave dinitro compounds, which on reduction were converted to the diamines [1].

It was interesting to determine the behavior of crotonic acid toward nitrogen tetroxide. If this reaction goes in the same manner as with ethylene hydrocarbons, then nitro compounds should be obtained, and their reduction should lead to the formation of the corresponding amino acids.

The action of nitrogen tetroxide on crotonic acid in ether solution gave the nitrite ester of nitrohydroxybutyric acid.* This compound when treated with water was converted to the crystalline α -nitro- β -hydroxybutyric acid.

Reduction of the nitrohydroxybutyric acid gave the amino acid, and then the corresponding hydrochloride. Crystals of α -aminobutyric acid were obtained when the aminohydroxybutyric acid was heated with hydriodic acid in a sealed tube.

Next we became interested in the problem of the mutual transformations of isocrotonic and crotonic acids. According to Egorov [2], the rearrangement takes place when the addition product is allowed to stand, but his conclusions lack experimental proof. The basis for Egorov's conclusions was obviously the cis-trans rearrangement hypothesis of Wislicenus [3], who expressed the theory that the isomerization is determined by the reversible process of addition and cleavage of the added substances.

Our investigations on the reaction of nitrogen tetroxide with crotonic and isocrotonic acids, and also with other unsaturated acids [4-10], and our observations on the behavior of the addition products during their formation and storage, do not agree with the opinions of Wislicenus and of Egorov. Our experiments, carried out under various conditions, revealed that isocrotonic acid is converted to crotonic acid irrespective of whether liquid or gaseous nitrogen tetroxide is used. In this connection the rearrangement went faster in ether solution than in the absence of solvent.

EXPERIMENTAL

A solution of 35.0 g of crotonic acid in 170 ml of dry ether was cooled to 0° and then saturated with nitrogen tetroxide (40.0 g) for 7 hr with cooling. When saturation was complete, the solvent was removed by passage of a stream of carbon dioxide through the solution. We obtained 70.3 g of a yellow oil, which was soluble in ether, ethyl acetate, alcohol, benzene, chloroform, acetone and dioxane, and insoluble in water, petroleum ether and ligroine. We obtained 30.7 g of crystals when the oil was allowed to stand with several drops of water. M. p. 122.5-123.5° (from ethyl acetate).

Found %: N 9.49, 9.20. M 151.60, 153.30. $C_4H_7O_5N$. Calculated %: N 9.40. M 149.

*A similar compound was obtained when isocrotonic acid was treated with nitrogen tetroxide.

When 2.0 g of the crystalline material was heated with 1.8 g of acetic anhydride on the water bath we obtained 1.3 g of crystals with m. p. 85–86° (from ethyl acetate).

Found %: N 7.22, 7.29. $C_6H_9O_6N$. Calculated %: N 7.35.

Reduction of 20.0 g of the nitrohydroxybutyric acid, employing the conditions used in the reduction of undecylenic acid [10], gave 3.4 g of aminohydroxybutyric acid with m. p. 230–231° (with decompn.). The hydrochloride of the aminohydroxybutyric acid was prepared; several drops of concd. hydrochloric acid (d 1.19) was added to a concentrated water solution of the acid, followed by the addition of alcohol and ether until a turbidity appeared. The next day the obtained crystals were separated, and washed with alcohol and then ether. M. p. 149–152°.

Found %: Cl 23.07. $C_4H_{10}O_3NCl$. Calculated %: Cl 22.80.

When a mixture of 1.0 g of the aminohydroxybutyric acid, 10 ml of hydriodic acid and some red phosphorus was heated in a sealed tube for 6 hr at 140–150° we obtained the aminobutyric acid with m. p. 271–272° (with decompn.).

From [11]: α -aminobutyric acid crystallizes as leaflets, melting at 272° (with decompn.); β -aminobutyric acid also crystallizes as leaflets, but it melts at 180° and deliquesces with ease when stored.

As a result, the acid obtained by us is identical with α -aminobutyric acid, which is indicated by the melting point and the fact that our acid does not deliquesce when stored, which is characteristic of the β -acid.

The problem of the mutual transformations of isocrotonic and crotonic acids was studied under various conditions. The experiments were run in parallel, using 2.0 g of isocrotonic and the same amount of crotonic acid, in ether and without a solvent, at a temperature of 0, +1, and 17–20°. In ether solution the isocrotonic acid isomerized immediately when 3–4 drops of the reagent was added. Without a solvent, the same amount of nitrogen tetroxide caused the isocrotonic acid to convert to crotonic acid in a matter of 13–15 min, while the addition of 7 drops of the reagent caused the isomerization to go in a matter of 3–5 min. That isocrotonic acid is converted to crotonic acid was confirmed by the change in both the melting point and the solubility. Before treatment the isocrotonic acid was a liquid, the solubility of which was 43.61 parts per 100 parts of water at 32–33°; the acid obtained after treatment with the reagent had m. p. 71–72° and a solubility of 10.12 parts per 100 parts of water at the same temperature; here in not a single case (from 19 experiments) were we able to detect the addition product. Consequently, isocrotonic acid converts to crotonic acid before nitrogen tetroxide adds to the double bond of the acid.

SUMMARY

1. Nitrogen tetroxide completely saturates the double bond in crotonic acid, in which connection the groups that add are ONO and NO_2 , differing from the olefins, which form dinitro compounds.
2. The crystalline α -nitro- β -hydroxybutyric acid was obtained, which was converted to the α -amino acid by reduction.
3. The problem of the mutual transformations of isocrotonic and crotonic acids under the influence of nitrogen tetroxide was investigated.

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ACTION OF NITROGEN TETROXIDE ON DIBENZALACETONE

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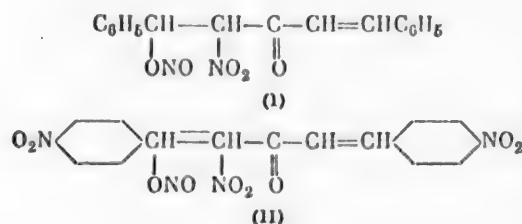
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On the example of the reaction of nitrogen tetroxide with unsaturated aliphatic ketones it was shown by one of us that, depending on the structure of the starting ketone, various addition products, differing in both their nature and properties, are obtained [1]. Here it was established that the nitro group adds to the least hydrogenated carbon atom, while the ONO group adds to the most hydrogenated carbon atom. When nitrogen tetroxide is reacted with benzalacetone the reactions that take place are not only addition to the double bond in the side chain, but also replacement of the hydrogen in the p-position of the benzene ring.

The problem of how dibenzalacetone would react with nitrogen tetroxide seemed of interest.

An ether solution of dibenzalacetone was treated with both gaseous and liquid nitrogen tetroxide. In the first case we obtained the nitrite ester of the nitro hydroxy ketone (I), while in the second case we obtained the nitrite ester of the trinitro hydroxy ketone (II).



When either the first or the second substance was shaken with water the ONO group was replaced by hydroxyl [2, 3], with the formation of the corresponding crystalline hydroxy nitro ketones. The addition products decomposed when heated on the water bath for 28-30 hr with either water or mineral acids [4, 5].

EXPERIMENTAL

a) A solution of 40.0 g of dibenzalacetone in 450 ml of ether, cooled to -1° , was saturated with nitrogen tetroxide (35.0 g) in 12 hr. On completion of reaction the solvent was removed by blowing with a stream of carbon dioxide. The brownish mass was treated with dry petroleum ether, and then with anhydrous methyl alcohol. After removal of the solvent we obtained 53.7 g of a yellow oil. The substance was soluble in ether, ethyl acetate, alcohol, and acetone; it was insoluble in water, petroleum ether, and benzene. Nitrous acid was cleaved when the substance was shaken with water.

Found %: N 8.10, 8.30. $\text{C}_{17}\text{H}_{14}\text{O}_5\text{N}_2$. Calculated %: N 8.60.

A mixture of 4.3 g of the substance and 100 ml of water was heated on the water bath for 8 hr. The mixture was then extracted with ether. The ether extract was dried over sodium sulfate. The solvent was removed by distillation. We obtained 1.7 g of plate crystals with m. p. $169-170^\circ$ (from benzene).

Found %: C 68.48, 68.39; H 5.2, 5.3; N 4.5, 4.6. $C_{17}H_{15}O_4N$. Calculated %: C 68.69; H 5.05; N 4.71.

Heating 3.8 g of the substance with 100 ml of water on the water bath for 28–30 hr led to decomposition of the molecule, in which connection we obtained 1.2 g of benzoic acid (m. p. 120–121°) and a small amount of benzaldehyde.

Reduction of the addition product. Into a water-cooled flask, fitted with a reflux condenser, dropping funnel and thermometer, was charged 120 g of tin. Then, with stirring, hydrochloric acid was added in small portions (5–10 ml), while the product (40.0 g) was added periodically in drops from the dropping funnel. When all of the components had been added the reaction flask was heated on the water bath for 5 hr. The residual tin was separated, while the liquid was diluted with 5 volumes of water and then treated with hydrogen sulfide. The stannous sulfide was filtered, while the filtrate was refluxed with 105 g of lead oxide. After removal of the lead chloride the mother liquor was again treated with hydrogen sulfide.

The filtrate from the lead sulfide was made alkaline and then was heated for 40 min on the water bath, after which it was extracted with ether. Benzyl alcohol (1.8 g) was isolated from the ether solution, and was characterized both by its boiling point of 204–205° and by oxidation to benzoic acid.

The water solution (after extraction with ether) was acidified with hydrochloric acid and then was evaporated to 1/2 volume. From the solution on cooling we obtained 8.7 g of benzoic acid with m. p. 120–121° (from water).

b) The dropwise addition of 32.0 g of nitrogen tetroxide to a solution of 25.0 g of dibenzalacetone in 280 ml of ether at $0 \pm 2^\circ$ was accompanied by a rise in temperature. The solution was brought back to the original temperature by cooling, and then additional nitrogen tetroxide was added, etc. On completion of reaction the solvent was removed by blowing with a stream of carbon dioxide; here the addition product decomposed violently with much heat evolution, leading to ignition. For this reason the substance was separated from the solvent, transferred to a separatory funnel, and washed in sequence with water and then petroleum ether. We obtained 32.0 g of liquid addition product, a substance that decomposed on storage, became thick, and burned explosively when held in a free flame.

The heating of 6.2 g of the liquid product with 100 ml of water gave 3.9 g of a crystalline trinitro hydroxy ketone. The yellow plates were soluble in both ether and alcohol, and insoluble in petroleum ether. M. p. 199–201° (from alcohol).

Found %: N 10.37, 10.70. $C_{17}H_{13}O_8N_3$. Calculated %: N 10.85.

A mixture of 5.6 g of the substance and 100 ml of water was heated on the water bath for 30 hr. Here we obtained 2.2 g of p-nitrobenzoic acid, m. p. 237–238° (from alcohol). The mixed melting point with the previously obtained p-nitrobenzoic acid was not depressed. As a result, long heating of the product with water, and also with mineral acids, leads not only to hydrolysis of the nitrogen-containing group, but also to a decomposition of the molecule.

An attempt to convert the nitro ketone to the amino ketone proved unsuccessful. We obtained 6.3 g of p-aminobenzoic acid (m. p. 184–185°) when 17.0 g of the product was reduced with tin and hydrochloric acid under the earlier described conditions.

SUMMARY

1. Dibenzalacetone adds nitrogen tetroxide to one double bond. Treatment with the gaseous reagent yields the nitrite ester of the hydroxy nitro ketone, while treatment with liquid nitrogen tetroxide leads to the formation of the nitrite ester of the hydroxy trinitro ketone. Here, besides the addition reaction, there is also replacement of the hydrogen in the p-position of the benzene ring.

2. The addition products decompose when heated with either water or mineral acids.

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REACTION OF NITROSOACETANILIDE WITH SOME ACID CHLORIDES

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It is known that nitrosoacetanilide in nonionizing solvents reacts in the tautomeric form, as benzenediazonium acetate. In harmony with this, it was shown by Waters [1] that the reaction products of nitrosoacetanilide with alkyl halides are acetic acid, nitrogen, and benzene halide.

In a previous paper [2] we expressed the opinion that the reactions investigated by Waters proceed with the intermediate formation of benzenediazonium halides, since when the reactions are run under milder conditions it is possible to isolate the benzenediazonium halides in up to 16% yield.

However, it must be emphasized that even under mild temperature conditions the course of the discussed reactions is extremely complex. This results in copious tar formation and the creation of secondary products (for example, biphenyl).

As far as we know, the reaction of nitrosoacetanilide with acid chlorides has not been studied before. Besides this, such an investigation is of interest in view of the high reactivity of the halogen in the discussed compounds.

Study revealed that the reaction of nitrosoacetanilide with benzoyl and p-toluoyl chlorides in an inert, nonionizing solvent (benzene) proceeds in a completely different manner. In contrast to the reactions with alkyl halides, the indicated reaction goes smoothly, without the formation of any secondary compounds or tarry products. The solvent does not take part in the reaction. The main reaction product is benzenediazonium chloride. Its yield is 67-76% of the theoretical:



The secondary reaction products are the mixed anhydrides of acetic and benzoic acids in the first case, and of acetic and p-toluic acids in the second case. However, due to their instability, only the symmetrization products of these anhydrides are extracted from the reaction mixture.

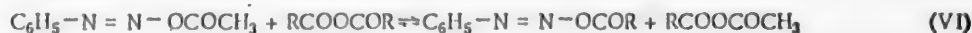
Apparently, the discussed reactions are not specific. The same result is obtained when nitrosoacetanilide is reacted with trimethylchlorosilane and with silicon tetrachloride, which have, as is known, a sharply expressed acid halide character. Together with the benzenediazonium chloride, trimethylsilicon acetate and tetraacetoxy-silane are formed in these reactions in good yields.



And finally, the reaction of nitrosoacetanilide with benzenesulfonyl chloride proceeds smoothly. However, pure benzenediazonium chloride cannot be isolated in this case; since the precipitate depositing from the benzene solution is a practically inseparable mixture of benzenediazonium chloride and the corresponding benzenesulfonic acid derivative.



The above given results can serve as still further evidence for the isomerization of nitrosoacetanilide to benzenediazonium acetate. In addition, the results of our study permit assuming that the acetyl group in the formed benzenediazonium acetate, even in nonionizing solvents of the benzene type, is quite labile, as a result of which the following reversible exchange reactions take place between the benzenediazonium acetate and carboxylic acid anhydrides.



In the case of acid chlorides reactions of this type cease to be reversible, since one of the products (benzenediazonium chloride) is practically insoluble in benzene and, consequently, is removed from the reaction sphere. For this reason it could be expected that other substances, having an anhydride character, will also react with nitrosoacetanilide in the same manner as acid chlorides, provided that one of the reaction products proves to be insoluble in the selected solvent.

To verify this postulation we studied the reaction of nitrosoacetanilide with *p*-toluenesulfonic anhydride. In harmony with the expressed ideas, the reaction goes in the direction of forming benzenediazonium tosylate and acetic anhydride.



The complexity of the decomposition of nitrosoacetanilide in alkyl halides has already been mentioned above. In a previous paper [2] we found that this process is even more complicated in the presence of hexaethylidistannane. In the latter case, together with the usual decomposition products, a number of new products appear and, in particular, the triethyltin halide. For this reason it seemed of interest to determine if the smooth course of the reaction of nitrosoacetanilide with acid chlorides is disturbed by the addition of hexaethylidistannane.

Besides the above described reaction of nitrosoacetanilide with acid chlorides, it proved that processes characteristic for the reaction of hexaethylidistannane with nitrosoacetanilide in the presence of alkyl halides are observed when hexaethylidistannane is added to a mixture of nitrosoacetanilide and *p*-toluoyl chloride. As a result, besides benzenediazonium chloride and the mixed anhydrides of acetic and *p*-toluic acids, the reaction products are nitrogen, triethyltin chloride, and a large amount of tarry products.

EXPERIMENTAL

Reaction of nitrosoacetanilide with benzoyl chloride. Nitrosoacetanilide (7.80 g) was dissolved in an ice-cooled solution of 6.70 g of benzoyl chloride in 30 ml of dry benzene. The mixture was kept in an ice-water bath for 24 hr. The crystalline precipitate of benzenediazonium chloride was filtered and then repeatedly washed with dry ether. We collected 5.2 g of carefully pressed, but not completely dry product, which was immediately dissolved in water. The water solution of benzenediazonium chloride was decomposed by heating to 50°, and was analyzed for HCl and phenol. The bromate-bromide titration method gave 3.09 g of phenol (2,4,6-tribromophenol, m. p. 96°), while the neutralization method gave 1.31 g of HCl. The yield of benzenediazonium chloride, based on the phenol, is 69.3%, while based on the HCl it is 75.6% of the theoretical.

The filtrate from the separation of the benzenediazonium chloride was combined with the rinse ether, and the whole was fractionated. We obtained 3.09 g of fraction I with b. p. 100–140°, and 4.2 g of fraction II with b. p. 170–172° at 3 mm.

Fraction I gave a positive test for acetic anhydride with 2,4-dichloroaniline [3]. The neutralization technique gave 2.28 g (47%) of the anhydride.

The treatment of 1.93 g of fraction II with alcoholic NaOH solution, followed by acidification with hydrochloric acid, gave 2.08 g of benzoic acid. The yield was quantitative, m. p. 121–122° (from water). The mixed

melting point with authentic compound was not depressed. Treatment of 1.56 g of fraction II with aniline in benzene medium gave 1.22 g (89.7%) of benzanilide with m. p. 162° (from benzene). The mixed melting point with authentic benzanilide was not depressed.

Judging by the properties, fraction II is benzoic anhydride. Yield 78.0%; m. p. 41° (from hexane). From [4]: m. p. 41–42°.

Reaction of nitrosoacetanilide with p-toluyol chloride. A solution of 7.67 g of nitrosoacetanilide and 7.22 g of p-toluyol chloride in 30 ml of dry benzene was kept in an ice-water bath for 48 hr. Using the above described procedure, we isolated 5.0 g of ether-moist benzenediazonium chloride. Yield 66.7% of the theoretical (established from the amount of HCl formed in the decomposition of a water solution of the benzenediazonium chloride).

The liquid portion of the reaction mixture was fractionated. Here we isolated a fraction with b. p. 100–140°. Analysis using 2,4-dichloroaniline revealed that this fraction contains 1.59 g (33.4%) of acetic anhydride [3].

The residue in the distillation flask crystallized when cooled. Two recrystallizations from alcohol gave 4.2 g (70.8%) of p-toluic anhydride with m. p. 93–94°. The mixed melting point with the authentic compound was not depressed. From [5]: m. p. 95°. Treatment of 1.06 g of the obtained anhydride with excess alcoholic NaOH solution, followed by removal of the alcohol by distillation and acidification of the residue with hydrochloric acid, gave 0.97 g of p-toluic acid. Yield 85.8%; m. p. 178–179° (from water). The mixed melting point with the authentic compound was not depressed.

Reaction of nitrosoacetanilide with benzenesulfonyl chloride. Nitrosoacetanilide (5.75 g) was dissolved in a cooled mixture of 6.23 g of benzenesulfonyl chloride and 25 ml of dry benzene. The mixture was kept in an ice bath for 48 hr. The crystalline product was filtered, repeatedly washed with dry ether, and immediately dissolved in water. The aqueous solution was decomposed at 50°, after which it gave a positive test for both chloride ion and phenol. Analysis of an aliquot sample established that 1.36 g of KOH is required to neutralize the solution. Evaporation of a second sample revealed that the solution contains 1.71 g of benzenesulfonic acid. Consequently, the crystalline product was a mixture of 2.83 g of $C_6H_5N_2OSO_2C_6H_5$ and 1.73 g of $C_6H_5N_2Cl$.

The liquid portion of the reaction mixture was fractionated in vacuo. Here we isolated 1.70 g of a fraction with b. p. 100–140°, which gave a positive test for acetic anhydride, and 2.70 g of unreacted benzenesulfonyl chloride. B. p. 119–122° at 12 mm. Benzenesulfonamide, m. p. 156° (from alcohol). The mixed melting point with authentic benzenesulfonamide was not depressed.

The yield of $C_6H_5N_2Cl$, based on reacted benzenesulfonyl chloride, was 61.6%; the yield of $C_6H_5N_2OSO_2C_6H_5$ was 54.0%.

Reaction of nitrosoacetanilide with silicon tetrachloride. A solution of 2.55 g of $SiCl_4$ in 40 ml of dry benzene was cooled in ice water. Then 9.84 g of nitrosoacetanilide was added. The mixture was cooled in ice for 4 days.

The benzenediazonium chloride was isolated in the usual manner. Yield 73.0% (determined from the amount of HCl formed in the decomposition of a water solution of the diazo compound).

The liquid portion of the reaction mixture was evaporated in vacuo. The residue was transferred to a flask with a narrow outlet tube and was vacuum-distilled twice. We obtained 1.38 g (52.2%) of product with b. p. 143–148° at 5 mm, and m. p. 108–109° (from ether).

For identification we synthesized tetraacetoxysilane by the Friedel–Ladenburg method [6]. The mixed melting point with the substance obtained by us was not depressed.

Reaction of nitrosoacetanilide with trimethylchlorosilane. A solution of 6.80 g of nitrosoacetanilide and 4.60 g of trimethylchlorosilane in 20 ml of dry benzene was cooled in ice water for 6 hr and then was allowed to stand at room temperature for 15 hr. The benzenediazonium chloride was filtered, washed with ether, and decomposed in water solution. Titration of the water solution by the bromate-bromide method gave 2.96 g of phenol (2,4,6-tribromophenol, m. p. 96°), while the neutralization method gave 1.34 g of HCl. The yield of benzenediazonium chloride, based on the phenol, is 76.0%, while based on the HCl it is 87.0%.

To determine the structure of the second product we ran the reaction in dry ether medium. The liquid portion of the reaction mixture, accumulated from 4 parallel experiments, was fractionated through a column. Calculated on the basis of one experiment, here we obtained 2.41 g (43.2%) of trimethylacetoxysilane with b. p. 101–103°; n_D^{20} 1.3893. From [7]: b. p. 102°, n_D 1.388.

Reaction of nitrosoacetanilide with p-toluenesulfonic anhydride. Nitrosoacetanilide (3.28 g) was added to a cooled solution of 3.26 g of p-toluenesulfonic anhydride in 40 ml of dry benzene. The mixture was allowed to stand with cooling in ice water for 3 days, after which the crystalline precipitate was filtered, washed with ether, and decomposed in water solution. The decomposition was accompanied by the evolution of nitrogen. Evaporation of a sample of the obtained solution in vacuo, followed by recrystallization of the residue from concd. hydrochloric acid, gave p-toluenesulfonic acid. M. p. 104–105°. The mixed melting point with the pure product was not depressed. Analysis of a second sample by the neutralization method gave 2.50 g of p-toluenesulfonic acid in the solution. Consequently, the yield of benzenediazonium tosylate is 72.6% of the theoretical.

Distillation of the liquid portion of the reaction mixture led to the isolation of a fraction with b. p. 90–140°, giving with 2,4-dichloroaniline a positive test for acetic anhydride.

Reaction of nitrosoacetanilide with p-toluoyl chloride in the presence of hexaethyldistannane. In a nitrogen stream, with external ice cooling, a charge of 27 ml of dry benzene, 4.24 g of p-toluoyl chloride, 3.48 g of hexaethyldistannane and 4.50 g of nitrosoacetanilide was loaded in the indicated order into an ampul with two outlet tubes.

The ampul was sealed and placed in an ice-water bath for 3 days. Considerable excess pressure was observed when the ampul was opened. In contrast to the previous experiments, the reaction mixture had a tarry appearance. The benzenediazonium chloride was isolated in the customary manner. Yield 0.46 g (12.1%). Then the reaction mixture was extracted with NaHCO_3 solution, washed with water, dried over CaCl_2 , and fractionated in vacuo. We isolated 1.90 g (46.5%) of triethyltin chloride with b. p. 95–98° at 15 mm, and n_D^{20} 1.5603. From [8]: b. p. 100–101° at 16 mm, and n_D^{20} 1.5055.

The voluminous tarry residue was recrystallized 3 times from alcohol to yield 1.81 g (52.1%) of p-toluic anhydride with m. p. 92–94°. The mixed melting point with the authentic substance was not depressed.

The mother liquors were combined, treated with alcoholic NaOH solution until alkaline, and then evaporated to dryness. Steam distillation of the residue led to the isolation of 0.02 g of biphenyl. M. p. 69° (from alcohol). The mixed melting point with authentic biphenyl was not depressed.

SUMMARY

A study was made of the reactions of nitrosoacetanilide with benzoyl chloride, p-toluoyl chloride, benzenesulfonyl chloride, trimethylchlorosilane and silicon tetrachloride in benzene solution.

It was shown that nitrosoacetanilide, reacting in the diazo form, smoothly exchanges the acetoxy group for chlorine when reacted with acid chlorides, or with compounds possessing an acid chloride character.

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* Original Russian pagination. See C. B. translation.

MESO DERIVATIVES OF ACRIDINE

XXIII. REACTION OF 9-METHYLACRIDINE WITH NITROSO COMPOUNDS*

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The reaction of 9-methylacridine with aromatic nitroso compounds has been studied many times. Thus, a compound with m. p. 231–232° was obtained when a mixture of 9-methylacridine and 4-nitrosodimethylaniline was heated in alcohol solution in the presence of sodium carbonate [1], which was assigned the structure of the azomethine. Two substances were isolated when 9-methylacridine was reacted with 4-nitrosodiethylaniline: the azomethine $C_{24}H_{23}N_3$ and a substance with the formula $C_{24}H_{23}N_3 \cdot H_2O$.

The fusion of 9-methylacridine with 4-nitrosodimethylaniline [2] led to the isolation of three substances: the azomethine with m. p. 244° and substances with m. p. 234° and 210–211°, both with the empirical formula $C_{22}H_{19}N_3 \cdot H_2O$.

Later it was found [9] that the azomethine is obtained in 85% yield when 9-methylacridine is heated with 4-nitrosodimethylaniline in alcohol solution, and also when 9-methylacridine is fused with 4-nitrosomonoethylaniline [4].

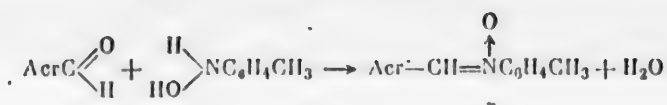
Later it was established that the heating of 9-methylacridine with 4-nitrosodimethyl-, diethyl- and monoethylanilines and nitrosobenzene in alcohol solution, in the presence of sodium carbonate, yields a mixture of the azomethine and the nitrone [5], while the reaction of 4-nitrosodimethylaniline with 9-methylacridine, 2-methoxy- and 2-methoxy-6-chloro-9-methylacridines yields nitrones, contaminated more or less with the azomethine [6].

The contradictory nature of the existing literature data caused us to make a study of several other reactions of 9-methylacridine with nitroso compounds: on the one hand, with such a simple aromatic nitroso compound as nitrosotoluene, and on the other hand, with a nitroso compound of the heterocyclic series, namely nitrosoantipyrine (1-phenyl-2,3-dimethyl-4-nitroso-5-pyrazolone), containing both tertiary nitrogen atoms and a carbonyl group. In addition, we examined the reaction of 9-methylacridine with nitrosophenol, a nitroso compound that is capable of tautomeric transformation to the isonitroso compound (quinone monoxime). In all cases the reaction was run under the conditions described in [1], i. e., in refluxing alcohol solution with the addition of sodium carbonate.

As the result of our experiments it was established that the reaction of 9-methylacridine with p-nitrosotoluene yields the nitrone; the yield of the nitrone depends on the amount of nitrosotoluene taken for reaction. We were unable to show the formation of noticeable amounts of the azomethine.

The structure of the obtained nitrone was confirmed by its synthesis from 9-acridinecarboxaldehyde and N-p-tolylhydroxylamine.

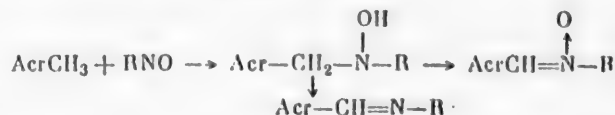
*For Communication XXII see Zhur. Obshchei Khim. 21, 1918 (1951).



The corresponding azomethine [9-(4'-methylphenyliminomethyl)-acridine] was obtained by the reaction of 9-acridinecarboxaldehyde with p-toluidine. Both the obtained nitrone and the azomethine are easily hydrolyzed in acid medium to yield 9-acridinecarboxaldehyde with m. p. 148°. The formation of neither the nitrone nor of any other compound is observed when the azomethine is heated with excess p-nitrosotoluene, and 90% of the starting azomethine is easily recovered from the reaction solution. This excludes the intermediate formation of the azomethine in the reaction of 9-methylacridine with p-nitrosotoluene.

The reaction of 9-methylacridine with p-nitrosophenol gave a compound with m. p. 227–228° (with decompn.), soluble in alkali. After purification the m. p. was 230° (with decompn.), and the analysis agreed with the structure of the corresponding nitrone. 9-Acridinecarboxaldehyde is formed when this compound is hydrolyzed with either 1% sulfuric or hydrochloric acid.

The corresponding azomethine [9-(4'-hydroxyphenyliminomethyl)-acridine] was obtained from p-azomethine and 9-acridinecarboxaldehyde. When this azomethine was heated with excess p-nitrosophenol we recovered 86% of the starting azomethine from the reaction. As a result, the same as in the case of the azomethine obtained from p-toluidine and 9-acridinecarboxaldehyde, excess nitroso compound does not affect the course of the reaction of the nitroso compound with 9-methylacridine and the azomethine is not converted by excess nitroso compound to the corresponding nitrone. From this it follows that the most probable scheme for the reaction of 9-methylacridine with nitroso compounds is the one that also satisfactorily explains the results obtained by us in the reaction of 9-methylacridine with 4-nitrosoantipyrine.



Here we isolated the azomethine with m. p. 228–229° as the main reaction product, and in addition we obtained a substance with m. p. 205–210° (with decompn.), which, based on the nitrogen analysis, corresponds to the composition of the binary compound of nitrone and azoxy compound. We were unable to isolate the nitrone in sufficiently pure form from this binary compound. We also synthesized the azomethine with m. p. 228–229° [9-(1'-phenyl-2',3'-dimethyl-5'-pyrazolone-4'-iminomethyl)-acridine] from 9-acridinecarboxaldehyde and 4-aminoantipyrine.

The results of our experiments indicate that the reaction of 9-methylacridine with nitroso compounds of diverse structure yields, depending on the nature of the taken nitroso compound, either the azomethine or the nitrone.

EXPERIMENTAL

9-Acridinyl-N-(4'-methylphenyl)-nitrone from 9-methylacridine and p-nitrosotoluene. A solution of 1.1 g of 9-methylacridine and 0.05 g of sodium carbonate in 10 ml of alcohol was prepared by heating to the boil. Then 0.7 g of p-nitrosotoluene was gradually added in 1 hour to the boiling solution and the mixture was heated for another 30 min. The reaction product crystallized as long yellow needles. Weight 0.6 g (33%), m. p. 215–217° (with decompn.). After recrystallization from either alcohol or benzene, m. p. 220° (with decompn.). The compound is readily soluble in chloroform, and difficultly soluble in ligroine and in ether. The compound is easily hydrolyzed in the presence of acids to yield 9-acridinecarboxaldehyde.

In a second experiment we obtained 0.18 g (55%) of the compound from 0.2 g of 9-methylacridine, 0.01 g of sodium carbonate, 5 ml of alcohol and 0.3 g of p-nitrosotoluene.

Found %: N 8.99, 8.89. $\text{C}_{21}\text{H}_{16}\text{ON}_2$. Calculated %: N 8.97.

In both experiments we isolated a certain amount of the starting substances from the mother liquors, but we were unable to detect the azomethine.

9-Acridinyl-N-(4'-methylphenyl)-nitron from 9-acridinecarboxaldehyde and N-p-tolylhydroxylamine.

A mixture of 0.2 g of 9-acridinecarboxaldehyde, 0.1 g of N-p-tolylhydroxylamine and 5 ml of alcohol was heated under reflux for 1 hour. The reaction mixture on cooling deposited yellow needles with m. p. 217° (with decompn.). Yield 0.22 g (73%). After recrystallization from alcohol, m. p. 220° (with decompn.). The mixed melting point with the nitron obtained from 9-methylacridine and p-nitrosotoluene was not depressed.

9-(4'-Methylphenyliminomethyl)-acridine from 9-acridinecarboxaldehyde and p-toluidine. A mixture of 0.2 g of 9-acridinecarboxaldehyde, 0.1 g of p-toluidine and 5 ml of alcohol was heated at the boil for about 1 hour. The solution on cooling deposited red prismatic crystals with m. p. 180–181°. Yield about 80%. After recrystallization from alcohol, m. p. 182–183°.

Found %: N 9.38, 9.55. $C_{21}H_{16}N_2$. Calculated %: N 9.46.

The azomethine is readily soluble in chloroform and in hot alcohol, and difficultly soluble in ether. The compound is hydrolyzed to 9-acridinecarboxaldehyde when refluxed with 10% hydrochloric acid. The azomethine is not converted to the corresponding nitron when treated with the nitroso compound, which can be seen from the following experiment: a mixture of 0.2 g of the obtained azomethine with m. p. 182–183°, 0.01 g of sodium carbonate and 8 ml of alcohol was heated to the boil and then 0.7 g of p-nitrosotoluene was added gradually to the boiling solution, followed by refluxing the mixture for about another 30 min. We isolated 0.18 g of unreacted azomethine, i. e. 90% of the taken amount, from the mixture on cooling.

9-Acridinyl-N-(4'-hydroxyphenyl)-nitron from 9-methylacridine and p-nitrosophenol. A mixture of 1 g of 9-methylacridine, 0.65 g of p-nitrosophenol, 0.01 g of sodium carbonate and 8 ml of alcohol was heated on the water bath at the boil for 2 hr. The obtained precipitate was filtered and washed several times with alcohol. We obtained 1 g of orange crystals (60%) with m. p. 227–228° (with decompn.). The compound is difficultly soluble in the common organic solvents, and is soluble in alkali. The compound was purified by dissolving in alkali, treating with animal charcoal, and then adding hydrochloric acid until the red precipitate of the hydrochloride appeared. Treatment of the hydrochloride with excess sodium carbonate solution gave the free base as a finely crystalline yellow precipitate with m. p. 230–231° (with decompn.). 9-Acridinecarboxaldehyde is formed when the compound is heated with either 1% sulfuric or hydrochloric acid. The use of excess nitrosophenol in this reaction does not improve the yield, since it leads to tar formation.

Found %: C 76.35, 76.55; H 4.85, 4.81; N 8.84, 8.91. $C_{20}H_{14}O_2N_2$. Calculated %: C 76.43; H 4.46; N 8.91.

9-(4'-Hydroxyphenyliminomethyl)-acridine from 9-acridinecarboxaldehyde and p-aminophenol. A mixture of 0.6 g of 9-acridinecarboxaldehyde, 0.3 g of p-aminophenol and 10 ml of alcohol was heated at the boil for 30 min. Orange crystals with m. p. 255° (with decompn.) were obtained. Weight 0.7 g (85.2%). The compound is difficultly soluble in the common organic solvents. 9-Acridinecarboxaldehyde is formed when the compound is heated with acids.

Found %: N 9.64, 9.76. $C_{20}H_{14}ON_2$. Calculated %: N 9.40.

The obtained azomethine is not converted to the nitron when treated with excess nitrosophenol, which can be seen from the following experiment: a mixture of 0.5 g of the azomethine, 0.02 g of sodium carbonate and 10 ml of alcohol was heated to the boil. Then 0.5 g of p-nitrosophenol was added gradually, in 1.5 hr. At the end of the reaction we isolated 0.43 g of the azomethine, or 86% of that taken for reaction.

9-[1'-Phenyl-2',3'-dimethyl-5'-pyrazolone-4'-iminomethyl]-acridine from 9-methylacridine and 4-nitrosoantipyrine. A mixture of 2.5 g of 9-methylacridine, 0.05 g of sodium carbonate and 20 ml of alcohol was heated to the boil and then 2.75 g of the nitrosoantipyrine was gradually added in 2 hr. The heating was continued for another 30 min. After several hours we collected 2.7 g (52.5%) of orange-red prisms with m. p. 220–221°. After recrystallization from alcohol, m. p. 228–229°. The compound is readily soluble in chloroform, moderately soluble in hot alcohol, and difficultly soluble in benzene and petroleum ether.

Found %: C 76.53, 76.57; H 4.89, 4.83; N 14.25, 14.20. $C_{25}H_{20}ON_4$. Calculated %: C 76.49; H 5.15; N 14.28.

Slender lilac-colored needles of the hydrochloride were obtained when the compound was treated with dilute hydrochloric acid in the cold.

Found %: N 13.13; Cl 8.15, 8.4. $C_{25}H_{20}ON_4 \cdot HCl$. Calculated %: N 13.05; Cl 8.28.

Treatment of the compound with 17-20% hydrochloric acid, even in the cold, results in the separation of the hydrochloride of 9-acridinecarboxaldehyde and sufficient heat evolution to complete the reaction.

The mother liquor from the separation of the azomethine was evaporated to remove the alcohol; the residue was recrystallized by dissolving in a little chloroform and then precipitating with petroleum ether. We obtained 2 g of crystals with m. p. 205-210° (with decompn.). The nitrogen content was: 16.77, 16.98 and 17.05%, which corresponds to the composition of the binary compound of nitrone and azoxy compound, formed from the nitrosoantipyrene. We were unable to isolate the free nitrone from this compound. We isolated 0.3 g of the starting 9-methylacridine from the petroleum ether.

9-[1'-Phenyl-2',3'-dimethyl-5'-pyrazolone-4'-iminomethyl]-acridine from 9-acridinecarboxaldehyde and 4-aminoantipyrene. A mixture of 0.2 g of 9-acridinecarboxaldehyde, 0.2 g of 4-aminoantipyrene and 5 ml of alcohol was heated at the boil for 1 hr. The obtained orange-red crystals were recrystallized from alcohol. M. p. 228-229°. The mixed melting point with the azomethine obtained from the condensation of 9-methylacridine with the nitrosoantipyrene was not depressed.

SUMMARY

1. It was established that nitrones are formed when 9-methylacridine is reacted with p-nitrosotoluene and p-nitrosophenol, while the azomethine is obtained as the main product when the reaction is with 4-nitrosoantipyrene.
2. Excess nitroso compound does not affect the reaction result, and the course of the reaction is determined by the properties of the starting nitroso compound.
3. The azomethines are easily obtained by reacting the proper amines with 9-acridinecarboxaldehyde.

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DERIVATIVES OF ACYLACETIC ESTERS
OF THE HETEROCYCLIC SERIES

III. SYNTHESIS OF α - AND β -THENOYLACETIC ESTERS, ARYLIDES,
AND AZOMETHINE DYES FROM THEM

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As a continuation of our work on the synthesis and study of the arylides of acylacetic acids of the heterocyclic series [1, 2], we synthesized the α - and β -thenoylacetic esters, arylides, and azomethine dyes from them.

α -Thenoylacetic ester was obtained by the ester condensation reaction from ethyl thiophenecarboxylate and ethyl acetate in the presence of sodium ethylate as the condensing agent [3]. β -Thenoylacetic ester is not reported in the literature. We obtained both the α - and β -thenoylacetic esters by the acylation of the ethoxymagnesium derivative of acetoacetic ester with the acid chlorides of the α - and β -thiophenecarboxylic acids, followed by cleavage of the corresponding thenoylacetoacetic esters with 5% alcoholic ammonia solution, employing the procedure described for the preparation of benzoylacetic ester [4].

The starting thiophenecarboxylic acids were obtained by reacting magnesium with either the 2- or the 3-halothiophene, followed by carboxylation of the obtained Grignard reagent [5, 6]. In turn, 2-iodothiophene was obtained by the iodination of thiophene in the presence of mercuric oxide [5], while 3-bromothiophene was prepared by the dehalogenation of 2,3,5-tribromothiophene employing the Steinkopf method [7] as modified by Gronowitz [6]. The α - and β -thenoyl chlorides were obtained by heating the appropriate thiophenecarboxylic acids with a large excess of thionyl chloride [8, 9].

The arylides of the α - and β -thenoylacetic acids were obtained by heating the proper thenoylacetic ester with an aromatic amine in o-xylene. The amines used by us were aniline, o-, m- and p-anisidine, o-, m- and p-chloroaniline, o-, m- and p-nitroaniline, and o-, m- and p-aminobenzoic acid. The obtained arylides are either colorless or faintly yellow crystals, soluble in alcohol, acetone and dioxane, and give a green-brown color with FeCl_3 in aqueous alcohol solution. The yields and properties of the obtained arylides are reported in Table 1.

From these data it can be seen that the introduction of either halogen or methoxy group in the benzene ring of the anilides of the α - and β -thenoylacetic acids causes a slight bathochromic shift of the absorption maximum. Introduction of the nitro group causes a slight bathochromic shift and the appearance in the case of the o-nitro derivatives of an additional absorption maximum, shifted toward the short wavelength region of the spectrum. The carboxyl group causes a substantial bathochromic effect in the case of the p-carboxy derivatives and the appearance of three absorption maxima with approximately equal extinctions in the wavelength limits: 215-220 $m\mu$, 250-255 $m\mu$, and 290-305 $m\mu$ for the o- and m-carboxy derivatives. In addition, it should be mentioned that the p-isomers of the chloro-, methoxy- and carboxyanilides of the α - and β -thenoylacetic acids show a greater absorption intensity than do the corresponding o- and m-isomers. A comparison of the ultraviolet absorption spectra of the arylides of α -thenoylacetic acid with those of the corresponding arylides of β -thenoylacetic acid reveals that the latter compounds, as a rule, show a lower intensity of absorption; exceptions are the o- and m-chloroanilides and the o-carboxyanilide of β -thenoylacetic acid.

TABLE 1

Arylides of α - and β -Thienoylacetic Acids of General Formula

Expt. No.	Position of substituent on benzene ring	R	Yield (in %)	Melting point	λ_{max}	ϵ_{max}	Empirical formula	Found (%)		
								C	H	N
1	α	C_6H_5	82	126.5°	250	30000	$\text{C}_{11}\text{H}_{11}\text{O}_2\text{NS}^a$	63.53,	4.51,	5.71,
2	β		80	122—123	250	26400		63.70, 63.54, 63.78	4.39, 4.42, 4.59	5.80, 5.78, 5.78
3	α	$\text{o-ClC}_6\text{H}_4$	71	102.5	255	9500		55.47,	3.74,	4.91,
4	β		71	121—122	255	23000		55.53, 55.48	3.60, 3.60	4.87, 5.19, 5.19
5	α	$\text{m-ClC}_6\text{H}_4$	80	104	255	12800	$\text{C}_{11}\text{H}_{10}\text{O}_2\text{NSCl}^b$	55.74,	3.29,	4.85
6	β		71	98.5	255	26000		55.67, 55.67, 55.80	3.44, 3.59, 3.66	4.78, 4.95
7	α	$\text{p-ClC}_6\text{H}_4$	81	138.5	255	50000		55.97,	3.85,	4.97,
8	β		76	134—135	255	36000		56.14, 55.63, 55.65	3.82, 3.67, 3.54	4.99, 5.22, 4.99
9	α	$\text{o-CH}_3\text{OC}_6\text{H}_4$	50	76.5—77	255, 290	22000, 18000		60.78,	4.77,	5.09,
10	β		47	64—65	255	6600		61.02, 60.78	4.54, 4.67	5.10, 5.23
11	α	$\text{m-CH}_3\text{OC}_6\text{H}_4$	78	108.5	255, 290	28000, 19600	$\text{C}_{11}\text{H}_{12}\text{O}_2\text{NSC}^c$	61.01,	4.72,	5.04,
12	β		64	71.5	255	7400		61.14, 60.74	4.71, 4.62	4.93, 5.05, 5.27
13	α	$\text{p-CH}_3\text{OC}_6\text{H}_4$	80	115.5	255	40000		60.84,	4.75,	5.04,
14	β		76	143.5	255	12400		60.84, 60.93, 60.96	4.72, 4.66, 4.46	5.01, 5.07, 5.22
15	α	$\text{o-NO}_2\text{C}_6\text{H}_4$	47	103.5	235, 260	21000, 18800		53.96,	3.42	9.52,
16	β		32	99—99.5	215, 255	12400, 13500		53.72, 53.63	3.69, 3.64	9.59, 9.55
17	α	$\text{m-NO}_2\text{C}_6\text{H}_4$	82	139.5	250	17200	$\text{C}_{11}\text{H}_{10}\text{O}_4\text{N}_2\text{S}^d$	53.46,	3.54,	9.62,
18	β		76	150.5	255	15600		53.65, 53.70, 53.80	3.63, 3.63, 3.73	9.66, 9.75, 9.96
19	α	$\text{p-NO}_2\text{C}_6\text{H}_4$	71	174	220, 265, 305	17200, 13000, 19200		54.00,	3.31,	
20	β		76	175	255, 315	16800, 25000		54.07,	3.49	
								53.52, 53.59	3.63, 3.49	9.76, 9.84

a Calculated %: C 63.65; H 4.52; N 5.71.

b Calculated %: C 55.81; H 3.60; N 5.01.

c Calculated %: C 61.07; H 4.76; N 5.09.

d Calculated %: C 53.78; H 3.45; N 9.65.

TABLE 1 (Continued)

Expt. No.	Position of substituent in thiophene ring	R	Yield (in %)	Melting point	λ_{\max}	τ_{\max}	Empirical formula	Found (%)		
								C	H	N
21	α	o-HOOCCH ₃	55	147-148	220, 255, 295	21000, 16400, 10100	C ₁₁ H ₁₁ O ₄ N ₂ C	58.18, 58.27	3.89, 4.04	5.16
22	β		42	142	215, 255, 300	25000, 18000, 7500		57.94	3.67	5.03, 4.95
23	α	m-HOOCCH ₃	59	212	225, 255, 290	37000, 24200, 14200		57.80, 57.82	3.80, 3.86	4.82, 5.02
24	β		60	212.5	220, 250, 305	22400, 20700, 9500		57.92, 57.96	3.81, 3.69	4.74, 4.78
25	α	p-HOOCCH ₃	68	234	270	31000		57.97, 58.03	3.76, 3.82	4.76, 4.87
26	β		68	278	265	24800		58.22, 58.21	4.01, 3.89	4.78, 4.74

A number of azomethine dyes were obtained by reacting the arylides of the α - and β -thenoylacetic acids with diethyl-p-phenylenediamine under oxidative condensation conditions in the presence of silver chloride [10]. The dyes were purified by chromatographing on aluminum oxide from chloroform solution and then were recrystallized from alcohol. The yields and properties of the obtained dyes are listed in Table 2.

A comparison of the spectrophotometric data for the azomethine dyes derived from the unsubstituted anilides of the α - and β -thenoylacetic acids with the data for the dyes derived from the chloro, methoxy- and nitro-anilides reveals that introduction of either chlorine or methoxy in the m- or p-position of the unsubstituted benzene ring of the anilide is practically without effect on the position of the absorption maximum, while introduction of the indicated groups in the o-position causes a slight hypsochromic effect. Introduction of the nitro group in any position causes some bathochromic shift of the absorption maximum.

It should be mentioned that for the azomethine dyes derived from the anilides of α -thenoylacetic acid the shift of the absorption maximum toward the long wavelength region of the spectrum is somewhat greater than for the azomethine dyes derived from the arylides of β -thenoylacetic acid; in addition, the latter compounds, as a rule, show a lower intensity of the absorption. Exceptions are the dyes derived from the o- and m-chloro- and the p-nitro-anilides of β -thenoylacetic acid.

An SF-4 spectrophotometer was used to record the ultraviolet absorption spectra of the arylides of the α - and β -thenoylacetic acids in alcohol solution, at a concentration of 0.5×10^{-4} M. An SF-2 spectrophotometer was used to record the spectra of the yellow azomethine dyes in alcohol solution, at a concentration of 0.4×10^{-4} M.

The spectrophotometric determinations were made by O. V. Glazunova, for which the authors wish to thank her.

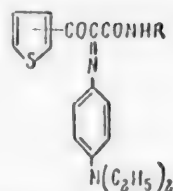
EXPERIMENTAL

β -Thenoylacetic ester. Anhydrous alcohol (15 ml) was added to 2.65 g of magnesium shavings. The reaction was started by the addition of 0.5 ml of carbon tetrachloride. Absolute ether (100 ml) was added in portions when vigorous reaction had subsided. The whole was stirred for 2-3 hr. The reaction mixture was then cooled to 5° and a solution of 13.0 g of acetoacetic ester in 20 ml of absolute ether was added dropwise with efficient stirring. After this, at 4-6° and with efficient stirring, a solution of 14.6 g of β -thenoyl chloride in 20 ml of absolute ether was added dropwise in 1 hour. The stirring was continued for another hour and then the mixture was allowed to stand overnight. The reaction mass was then treated with a mixture of ice and dilute sulfuric acid, followed by separation of the ether layer, which was then washed with water, dried over sodium sulfate, and the ether removed by distillation. The residue, being nearly pure β -thenoylacetoacetic ester, was then

*Calculated %: C 58.10; H 3.83; N 4.84.

TABLE 2

Azomethine Dyes of General Formula



Expt. No.	Position of substituent in thiophene ring	R	Yield (in %)	Melting point	Color of crystals	λ_{\max}	ϵ_{\max}	Empirical formula	Found % N
1	α	C_6H_5	32	184.5—185.5°	Red-brown	454	62000	$C_{22}H_{20}O_2N_2S^a$	10.41,
2	β		27	183.5—184	Red-brown	440	46500		10.41,
3	α	$o\text{-ClC}_6\text{H}_4$	38	148.5	Yellow-red	444	61000		9.95,
4	β		31	113	Yellow	441	68000		10.56
5	α	$m\text{-ClC}_6\text{H}_4$	29	149—149.5	Red	458	61000	$C_{22}H_{19}O_2N_2S^{cb}$	9.75,
6	β		30	141—141.5	Yellow-red	448	63000		9.82
7	α	$p\text{-ClC}_6\text{H}_4$	34	176—176.5	Yellow-red	455	54500		9.66,
8	β		24	193.5—194	Yellow-red	440	39000		9.72
9	α	$o\text{-CH}_3\text{OC}_6\text{H}_4$	38	143—144	Yellow-red	441	59500		9.73,
10	β		36	94.5—95.5	Yellow	437	48500		9.76
11	α	$m\text{-CH}_3\text{OC}_6\text{H}_4$	25	138—138.5	Yellow-red	453	48000	$C_{22}H_{19}O_2N_2S^c$	9.64,
12	β		23	142—142.5	Yellow-red	439	34500		9.57
13	α	$p\text{-CH}_3\text{OC}_6\text{H}_4$	27	144—145	Yellow	456	57000		9.56
14	β		22	142—143	Yellow	439	54500		9.62,
15	α	$o\text{-NO}_2\text{C}_6\text{H}_4$	32	177.5	Red	460	54500		9.72
16	β		31	165.5—166	Red	458	44500		9.48,
17	α	$m\text{-NO}_2\text{C}_6\text{H}_4$	34	170—170.5	Red	458	80000	$C_{22}H_{17}O_2N_4S^d$	9.66
18	β		26	163.5—164	Yellow	443	51000		9.46,
19	α	$p\text{-NO}_2\text{C}_6\text{H}_4$	27	206.5—207	Yellow	460	49000		9.47
20	β		21	188.5—189	Yellow	452	58000		9.61,
									9.76
									12.15,
									12.30
									12.43,
									12.20
									12.20,
									12.28
									12.15,
									12.15
									12.17,
									12.18
									12.77,
									12.69

a Calculated % N 10.7.

b Calculated % N 9.55.

c Calculated % N 9.65.

d Calculated % N 12.43.

treated with 5% alcoholic ammonia solution at 0° for 10–12 hr. At the end of this time a part of the alcohol was distilled off, while the residue was treated with a mixture of ice and dilute sulfuric acid, followed by extraction with ether, after which the ether extract was washed with water, the ether distilled off, and the residue was fractionated. Yield 65%, b. p. 162–175° at 12 mm; an aqueous alcohol solution of the compound gives a crimson color with FeCl_3 .

α -Thenoylacetic ester. The compound was obtained in the same manner as the β -isomer. Yield 69%, b. p. 140–143° at 4 mm; a crimson color is obtained when an aqueous alcohol solution of the compound is treated with FeCl_3 .

o -Chloroanilide of α -thenoylacetic acid. A mixture of 2.97 g of α -thenoylacetic ester, 1.9 g of o -chloroaniline and 30 ml of o -xylene was heated to 145° and then, with stirring, 20 ml of the solvent was distilled off, after which the mixture was cooled to 90–100° and another 8 ml of solvent was removed by vacuum-distillation. The residue was washed with ether and then recrystallized from aqueous methanol. Yield 71%, m. p. 102.5°.

The other arylides of the α - and β -thenoylacetic acids, listed in Table 1, were synthesized in a similar manner.

Azomethine dye from o -chloroanilide of α -thenoylacetic acid. A solution of 3.06 g of AgNO_3 in 14 ml of water was added with stirring to a solution of 1.16 g of NaCl in 14 ml of water. The obtained suspension of AgCl was treated with a solution of 1.4 g of Na_2CO_3 in 7 ml of water and a solution of 0.56 g of the o -chloroanilide of α -thenoylacetic acid in 20 ml of methanol. Then a solution of 0.58 g of diethyl- p -phenylenediamine sulfate in 14 ml of water was added with stirring to the reaction mass in 10–15 min. The stirring was continued for 1 hour. The precipitate was filtered, dried at 50–60°, extracted with chloroform, chromatographed on aluminum oxide from the chloroform solution, and recrystallized from methanol. Yield 38%, m. p. 148.5°.

A number of other azomethine dyes, the properties of which are given in Table 2, were synthesized in a similar manner.

SUMMARY

1. Acylation of the ethoxymagnesium derivative of acetoacetic ester with the acid chlorides of α - and β -thiophenecarboxylic acids, followed by ammonolysis of the obtained α - and β -thenoylacetoacetic esters, gave the α - and β -thenoylacetic esters.
2. The corresponding arylides were synthesized by reacting the α - and β -thenoylacetic esters with aniline, o -, m - and p -chloroaniline, o -, m - and p -nitroaniline, o -, m - and p -anisidine, and o -, m - and p -aminobenzoic acid, and their properties were studied.
3. Yellow azomethine dyes were synthesized by reacting the arylides of the α - and β -thenoylacetic acids with diethyl- p -phenylenediamine under oxidative condensation conditions in the presence of silver chloride, and their properties were studied.

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FORMATION OF POLYAMIDE RESINS

XI. PREPARATION OF POLYAMIDES EMPLOYING INTERFACIAL POLYCONDENSATION

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The recently proposed method of obtaining polymers by interfacial polycondensation [1] differs from previously used polycondensation methods not only in the reaction conditions employed, but also in the nature of the starting compounds. Thus, polyamides of the type of nylon 66 and capron are respectively synthesized from diamines and dicarboxylic acids and from caprolactams, while polyurethans are obtained from diisocyanates and glycols. For interfacial polycondensation to go successfully in the formation of polyamides it is necessary to replace the dicarboxylic acid by the acid chloride, while in the preparation of urethans the diisocyanates and glycols are replaced by diamines and the chlorocarbonic esters of glycols.

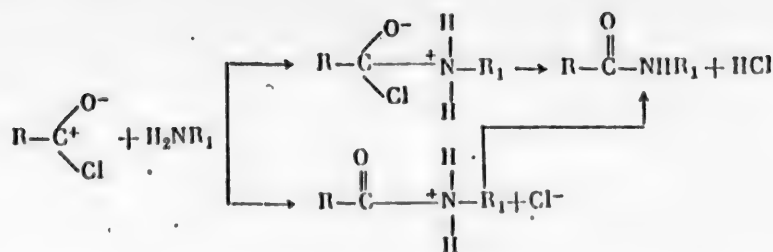
It should be mentioned that diamines and the chlorocarbonic esters of glycols have been proposed for the synthesis of polyurethans [2] employing conventional polycondensation. However, such syntheses have not found wide acceptance, possibly because of the insufficiently high molecular weight of the reaction products.

Polymers with a high molecular weight are formed very rapidly and at a comparatively low temperature when the interfacial polycondensation method is employed. Since this method had also been used for the synthesis of polyamides, the mechanism for the formation of which we had studied earlier, we deemed it expedient to determine whether our concepts regarding the formation of a polyamide could be extended to the process for its formation employing interfacial polycondensation.

In investigating this polycondensation method we also examined the problem of the influence exerted by the structure of the starting compounds on the reaction. This problem deserves consideration for the reason that, in contrast to ordinary polycondensation, low yields of polymers are observed with certain starting compounds, and the structure of the monomers could be a reason for such a phenomenon.

Earlier we had indicated [3] that the mechanism of any reaction for the formation of polyamides can be explained by the B. A. Porai-Keshits scheme [4], which is based on the ability of the carbonyl group of the carboxylic acid, due to its polarizability, to add the nitrogen of ammonia or amino group.

In the case of interfacial polycondensation the carboxylic acids are replaced by the acid chlorides. It must be assumed that replacing the hydroxyl group of the carboxyl by chlorine and the absence of the possibility to dissociate greatly enhances the electron-acceptor activity of the carbon atom of the acid chloride. Only in this manner is it possible to explain the successful progress of the reaction at room temperature, whereas high temperatures are required for other cases of amidation. For this reason the scheme of the amidation reaction during interfacial polycondensation should not differ in principle from the discussed schemes and may be depicted in the following manner.



In this connection it should be mentioned that all that has been said before regarding polymerization (hydrolytic) and polycondensation reactions in the formation of polyamide resins from caprolactam in the presence of water has not lost its significance [5]. It is only necessary to remember that a similar separation of the reactions is accomplished on the basis of a formal criterion and that the mechanism of both reactions is analogous [3].

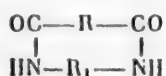
From an examination of various cases of amidation it follows that the activity of the functional groups exerts, as was to be expected, a great influence on the reaction rate. Thus, in the case of reacting phenylenediamines and carboxylic acids, due to the low basicity of aromatic amines, the reaction goes successfully only in the presence of mineral acid [4]. In the formation of polyamides by the reaction of aliphatic diamines and dicarboxylic acids the presence of mineral acids, due to the greater activity of the functional groups of the diamines, is no longer needed, but a high temperature is still required. In alkaline polymerization, due to the even higher activity of the functional groups, a further increase in the reaction rate is observed [3]. Finally, in the case of the acid chlorides of carboxylic acids the functional group is so active that the amidation, as is the case in interfacial polycondensation, goes at room temperature.

Consequently, the mechanisms for the processes of conventional amidation and amidation at the interface are analogous.

We had already mentioned that the yields of polyamide in interfacial polycondensation are low in some cases. In investigating the reasons for this phenomenon we found that the yield of the polymer increases with increase in the number of carbon atoms in the acid chloride or if one of the linear components is replaced by a cyclic compound.

When an acid chloride with a large number of carbon atoms is used, for example sebacoyl chloride, not only the yield, but also the viscosity of the polymer is increased.

Further investigation of the process for the reaction of linear components revealed that in this case a cyclic compound is formed along with the polymer.



Similar to the cyclic dimer and trimer of caprolactam [6], this cyclic compound has a high melting point. As a result, it is obvious that one of the reasons for low yields of the polymer in the interfacial condensation of linear monomers is because the reaction goes in two directions—with the formation of linear polymers and of low-molecular cyclic compounds.

As was indicated above, using sebacoyl chloride in the reaction makes it possible to obtain quite high yields of the polymer even with a linear diamine.

The cyclic diamide is readily soluble in alcohol, and difficultly soluble in acetone and in ether.

To obtain larger amounts of the cyclic compounds we reacted adipoyl chloride and hexamethylenediamine by the technique of mixing their benzene solutions, i. e., not at the interface of two phases. In order that neutralization of the hexamethylenediamine by the liberated hydrogen chloride did not cause a decrease in the yield of cyclic compound, the amount of hexamethylenediamine in the solution was taken in a molar ratio twice that of the adipoyl chloride. Despite this, the benzene-insoluble reaction product was found to contain, besides polymer and cyclic compound, a substantial amount of hexamethylenediamine, which had failed to react either with the adipoyl chloride or with the hydrogen chloride. Evidently, the described conditions are not favorable for complete reaction of the components.

The cyclic structure of one of the components of the reaction excludes the progress of secondary processes analogous to the one just described, which leads to a sharp increase in the yield of the polymer. We observed especially high yields of the polymer when sebacoyl chloride was reacted with piperazine. As a result, the structure of the starting components exerts a large influence on the yields of the polymers obtained by the technique of interfacial polycondensation.

EXPERIMENTAL

1. Polycondensation of linear components. a) Adipoyl chloride (0.52 g) was dissolved in 50 ml of chloroform (0.0586M); 2.25 g of hexamethylenediamine was dissolved in 50 ml of water (0.39M); 1.56 g of NaOH was added to the latter solution (0.78M). Then the two solutions were mixed and the obtained precipitate contained 0.25 g of polymer (36.36%), based on the adipoyl chloride. The viscosity of a 0.5% solution of the polymer in tricresol was η_{sp} 0.1393.

b) Equimolar ratios of adipoyl chloride and hexamethylenediamine were taken; the yield of polymer was 40%; η_{sp} 0.295.

c) Benzene was used as the solvent; the adipoyl chloride was replaced by sebacoyl chloride; the ratios of the components were the same as in a). The yield of polymer was 91%; η_{sp} 0.614.

2. Polycondensation of linear and cyclic components. a) Terephthaloyl chloride (1.189 g) was dissolved in 100 ml of ether (0.0586M); 4.524 g of hexamethylenediamine was dissolved in 100 ml of water (0.39M); 3.12 g of NaOH was added to the latter solution (0.78M). The yield of polymer was 1.078 g, i. e. 79%, based on the terephthaloyl chloride; because of its insolubility in tricresol the viscosity of the polymer was not determined.

b) The reaction components were adipoyl chloride and piperazine. The solvent for the adipoyl chloride was benzene. The ratios of the components were the same as in a). The yield of polymer was 95%; η_{sp} 0.392.

c) The reaction components were sebacoyl chloride and piperazine. The solvent was chloroform. Sebacoyl chloride (1.088 g) was dissolved in 10 ml of chloroform (0.234M); 1.696 g of piperazine was dissolved in 10 ml of water (1.36M); 1.088 g of NaOH was added to the latter solution (2.72M). The yield of polymer was 0.58 g, i. e. 85%, based on taken acid chloride. The viscosity of the polymer was η_{sp} 0.91.

3. Isolation of cyclic product from the reaction of linear dicarboxylic acid chloride and linear diamine. Benzene solutions of adipoyl chloride and hexamethylenediamine, taken in a molar ratio of 1 : 2, were mixed and the obtained precipitate was filtered and washed with benzene until all of the hexamethylenediamine had been removed. Then the precipitate was digested with alcohol and the alcohol extract was diluted with ether. Here a copious precipitate of hexamethylenediamine hydrochloride deposited, which was filtered. The alcohol-ether mixture was evaporated. The obtained crystalline precipitate proved to be insoluble in ether, and difficultly soluble in acetone. It was readily soluble in alcohol and in alcohol-ether mixture. Employing known titration methods [7], the presence of functional groups in the crystalline precipitate could not be detected. The product darkened at 210° and melted at 239–240°.

Found %: C 63.74; H 9.99; N 12.59. M 230. $C_{12}H_{22}O_2N_2$. Calculated %: C 63.71; H 9.73; N 12.38. M 226.

A compound with similar properties and a similar composition was also isolated from the alkaline aqueous solution after removal of the polymer, obtained by the technique of interfacial polycondensation, from it by filtration.

SUMMARY

1. The process of polycondensation at the interface of two immiscible liquids represents a reaction the mechanism of which is analogous to the mechanism of the conventional amidation reaction.

2. The structure of the starting components exerts a large influence on the yield of the polyamide obtained by the technique of interfacial polycondensation.

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NEW SYNTHESIS OF 5,6-DIMETHYLBENZIMIDAZOLE

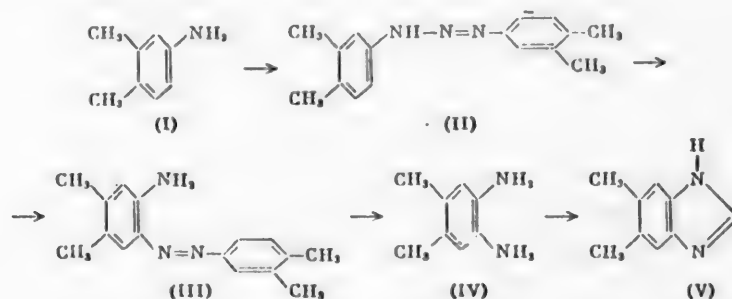
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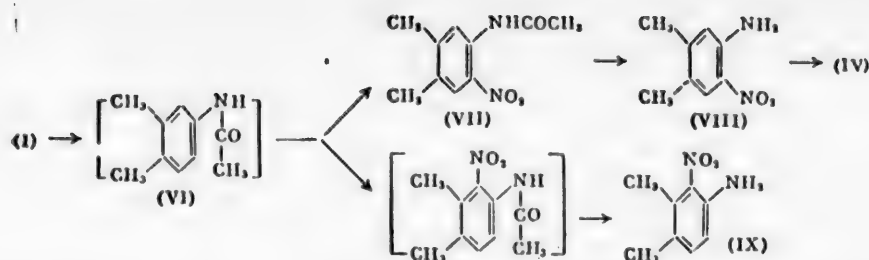
5,6-Dimethylbenzimidazole is a structural element of the vitamin B₁₂ molecule. The presence of 5,6-dimethylbenzimidazole in the culture medium of propionic acid microorganisms facilitates the directed biosynthesis of vitamin B₁₂ and increases its yield.

Several methods are known for the synthesis of 5,6-dimethylbenzimidazole, which suffer from the disadvantage that isomeric compounds are obtained as by-products in the intermediate stages of the synthesis. One of the methods for obtaining 5,6-dimethylbenzimidazole starts with 3,4-xylydine, which is nitrated [1] to 5-nitro-4-amino-o-xylene using a mixture of nitric and sulfuric acids at -15°. Here a mixture of still two other isomeric derivatives of the xylydine is formed along with the 5-nitro-4-amino-o-xylene, which is obtained in 39% yield. The 5-nitro-4-amino-o-xylene is reduced [2, 3] either with tin in concd. hydrochloric acid or with zinc dust in water to 4,5-diamino-o-xylene, which is then condensed with formamide or with formic acid in the presence of hydrochloric acid to 5,6-dimethylbenzimidazole [4, 5].

We developed a new synthesis of 5,6-dimethylbenzimidazole (V) from 3,4-xylydine (I), which consisted in the conversion of (I) to diazoamino-3,4-dimethylbenzene (II), and the latter was rearranged to 3,4-dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene (III). The o-aminoazo dye (III) was reduced to 4,5-diamino-o-xylene (IV), which was then condensed with formic acid to give 5,6-dimethylbenzimidazole (V) in an over-all yield of 42%.



The structure of the 3,4-dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene (III) was shown by its cleavage by catalytic hydrogenation to 3,4-xylydine (I) and 4,5-diamino-o-xylene, identical with the substance obtained by direct synthesis from 3,4-xylydine (I) through its acetyl derivative (VI), which was converted to 5-nitro-4-acetamido-o-xylene (VII) and then to the known 6-nitro-3,4-xylydine (VIII). 2-Nitro-3,4-xylydine (IX) was isolated as a by-product in this synthesis.



The conditions used to nitrate the acetylxylidine (VI) were such as to shift the direction of the reaction toward the formation of the desired isomer (VII).

EXPERIMENTAL

Diazoamino-3,4-dimethylbenzene (II). a) A solution of 10 g of 3,4-xylidine in a mixture of 20 ml of concd. hydrochloric acid and 14 ml of water was cooled to 2°, after which 10 g of ice was added, and then a solution of 2.9 g of sodium nitrite in 4 ml of water (3–5°). After this, 60 ml of 28% sodium acetate solution was added to the reaction mixture and the whole was allowed to stand at 15–20° for 2 hr. The obtained yellow precipitate was filtered and repeatedly washed with water. We obtained 9.55 g (91%) of diazoamino-3,4-dimethylbenzene as yellow prisms with m. p. 141–142° (with decompn.) (from alcohol). The substance has an absorption maximum in the ultraviolet region at 360 mμ $\epsilon 2.22 \times 10^4$ (in alcohol).

Found %: C 75.80, 75.63; H 7.77, 7.83; N 16.74, 16.54. $C_{16}H_{19}N_3$. Calculated %: C 75.85; H 7.56; N 16.58.

b) A solution of 5 g of 3,4-xylidine in a mixture of 15 ml of concd. hydrochloric acid and 15 ml of water was poured over 25 g of ice and then diazotized with a solution of 2.85 g of sodium nitrite in 7 ml of water. Then the diazonium salt solution was added to a solution of 5 g of 3,4-xylidine in a mixture of 10 ml of concd. hydrochloric acid and 60 ml of water, followed by the addition of 60 ml of 28% sodium acetate solution. The reaction mixture was kept for 2 hr at 15–20°, after which the obtained yellow precipitate was filtered and washed with water. We obtained 9.7 g (92.9%) of diazoamino-3,4-dimethylbenzene with m. p. 141–142° (with decompn.) (from alcohol).

3,4-Dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene (III). A mixture of 10 g of diazoamino-3,4-dimethylbenzene (II), 30 g of 3,4-xylidine and 4 g of 3,4-xylidine hydrochloride was stirred at 35° for 3.5 hr. Here the reaction mass, initially having the appearance of a melt, began to deposit an orange precipitate of the o-aminoazo dye (III). Then the reaction mass was stirred for 5 hr at 40–45° and for 5 hr at 45–50°; the precipitate was filtered (at 30°) and washed twice with 5 ml portions of alcohol. We obtained 6.8 g (68%) of 3,4-dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene as yellow plates with m. p. 185–186° (from alcohol). From [6]: m. p. 179°. The absorption spectrum of the substance exhibits the maxima: 327 mμ ($\epsilon 1.82 \times 10^4$) and 436 mμ ($\epsilon 0.98 \times 10^4$).

Found %: C 75.63, 75.96; H 7.36, 7.32; N 16.39, 16.40. $C_{16}H_{19}N_3$. Calculated %: C 75.85; H 7.56; N 16.58.

4,5-Diamino-o-xylene (IV) from o-aminoazo dye (III). A solution of 10 g of 3,4-dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene (III) in 50 ml of alcohol was hydrogenated in the presence of 8 g of skeletal nickel catalyst for 3 hr at 60–70° and a pressure of 50 atm. Then the catalyst was filtered, the solvent removed by distillation, the 3,4-xylidine (3.1 g with m. p. 47°) removed by steam distillation, and the residual aqueous solution was filtered hot. The filtrate on cooling deposited a precipitate, which was filtered. We obtained 4.2 g (78.5%) of 4,5-diamino-o-xylene with m. p. 126–127°. The mixed melting point with the substance obtained from 5-nitro-4-amino-o-xylene was not depressed.

Found %: C 70.46, 70.47; H 8.66, 8.60; N 20.6, 20.90. $C_8H_{12}N_2$. Calculated %: C 70.55; H 8.88; N 20.57.

5,6-Dimethylbenzimidazole (V). A mixture of 36 g of 4,5-diamino-o-xylene (IV), 72 ml of formic acid, 180 ml of water and 90 ml of hydrochloric acid (d 1.19) was heated under reflux (temperature about 130°) for 2 hr. On conclusion of reaction the mixture was heated with 2 g of decolorizing carbon and then filtered.

On standing in the cold the reaction mixture deposited the crystalline hydrochloride of 5,6-dimethylbenzimidazole, which was filtered, washed with water, and dried. We obtained 34.4 g (71.4%) of substance as colorless needles (do not melt at 320°). The substance was dissolved in 120 ml of water with gentle warming and then the 5,6-dimethylbenzimidazole was precipitated from the solution by the addition of about 20 ml of ammonia (until the odor of ammonia persisted). We obtained about 26.8 g of 5,6-dimethylbenzimidazole as colorless or slightly colored needle crystals with m. p. 204–205°.

Found %: C 73.97, 74.13; H 6.89, 6.90. $C_{11}H_{10}N_2$. Calculated %: C 73.97; H 6.85.

The acid mother liquor after isolation of the 5,6-dimethylbenzimidazole hydrochloride was treated with ammonia solution until neutral to Congo, and then ammonia solution was added in drops to precipitate the flocculent impurities, which were filtered. Then the 5,6-dimethylbenzimidazole was precipitated by the further addition of ammonia. We obtained a total of 32.7 g (84.8%) of the compound. 5,6-Dimethylbenzimidazole can be recrystallized from boiling water, using the aqueous mother liquor to dissolve the starting product a second time.

If the substance has a low melting point it can be purified by dissolving in 10% hydrochloric acid and subsequent precipitation with either ammonia or sodium hydroxide solution.

This procedure was used to obtain 5,6-dimethylbenzimidazole (m. p. 204–205°) from the 4,5-diamino-o-xylene synthesized from 5-nitro-4-amino-o-xylene.

5-Nitro-4-acetamido-o-xylene (VII). Acetic anhydride (45 ml) was added to 50 g of 3,4-xylylidine; the reaction was accompanied by self-heating up to 100–120°. The mixture was heated with periodic stirring at 100–120° for 1 hour, after which 40 ml of 98% acetic acid was added and the mixture cooled to 10–20°.

The above prepared solution of 4-acetamido-o-xylene (VI) in acetic acid was added in 1 hour to a nitration mixture of 45 ml of 57% nitric acid and 45 ml of sulfuric acid (d 1.83), cooled to 10°. During the nitration the temperature of the reaction mass was kept at 10–18° by external cooling. On conclusion of reaction the mixture was kept at the same temperature for 1 hour, at the end near 30°. Then 250 ml of water was added to the reaction mass with stirring. Usually a yellow precipitate of the 5-nitro-4-acetamido-o-xylene deposited immediately when about 50 ml of the water had been added; in such case the water addition was stopped for several minutes (to form coarser crystals), after which the rest of the water was added and then the precipitate was stirred with the liquid for 30–40 min. On obtaining a homogeneous mass the precipitate was filtered, washed well with water (200–300 ml), pressed, and dried. We obtained 58.4 g (68.0%) of 5-nitro-4-acetamido-o-xylene (VII) as yellow needle crystals with m. p. 97–100°. After recrystallization from alcohol, m. p. 106–107°. From [1]: m. p. 106–107°.

On long standing, the aqueous mother liquor from the isolation of the 5-nitro-4-acetamido-o-xylene deposited 5.7 g (6.7%) of oily nitration products, which proved to be soluble in alcohol. From this oily product after deacetylation and dilution with water we obtained 0.8 g of 3-nitro-4-amino-o-xylene (IX) as orange-red crystals with m. p. 65–66° (from aqueous alcohol, 1 : 1). From [1]: m. p. 65–66°.

5-Nitro-4-amino-o-xylene (VIII). A mixture of 175 ml of hydrochloric acid (d 1.19) and 70 g of 5-nitro-4-acetamido-o-xylene (VII) was heated on the water bath for 2 hr, after which it was cooled and diluted with 3 volumes of water with stirring. The obtained precipitate of 5-nitro-4-amino-o-xylene was filtered, washed well with water, pressed, and dried. We obtained 43.9 g (78.5%) of 5-nitro-4-amino-o-xylene as orange-red crystals with m. p. 136–138°.

4,5-Diamino-o-xylene (IV) from nitroxylylidine (VIII). A suspension of 60 g of 5-nitro-4-amino-o-xylene (VIII) in 540 ml of 85–96% alcohol was hydrogenated in the presence of 24 g of skeletal nickel catalyst for 2 hr at 40–45° and a pressure of 60–35 atm. At the end of reaction the solution was heated to 60–70° and the catalyst was removed by filtration.

The filtrate on cooling deposited 4,5-diamino-o-xylene; the product was filtered, pressed well, washed with alcohol, and dried. The solvent was distilled (in vacuo) from the mother liquor, and additional compound was isolated from the residue. We obtained 41.8 g (85.1%) of 4,5-diamino-o-xylene as dark plates with a mother-of-pearl luster, and having m. p. 126–127°.

SUMMARY

5,6-Dimethylbenzimidazole was synthesized in good yield by a new technique from 3,4-xylydine, through the intermediates 3,4-dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene and 4,5-diamino-o-xylene.

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REACTIONS OF ESTERS OF AROMATIC SULFONIC ACIDS

IX. REACTION OF 2,4-DINITROPHENYL BENZENESULFONATE

WITH ALIPHATIC AMINES

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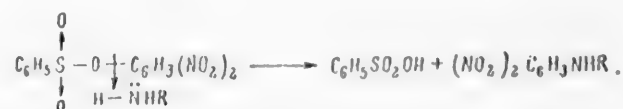
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In the previous paper [1] it was shown that aryl sulfonates, containing either the 2-nitro- or the 2,4-dinitro- group in the phenol portion of the ester exhibit arylating properties when reacted with aromatic amines. In the present paper we investigated the reaction of 2,4-dinitrophenyl benzenesulfonate with the aliphatic amines—methylamine, dimethylamine, ethylamine, diethylamine, isopropylamine, butylamine, benzylamine, benzylamine, and piperidine.

A comparison of the experimental data reveals that when 2,4-dinitrophenyl benzenesulfonate is reacted with aliphatic amines the main direction of the reaction is aryl-oxygen fission, while the mechanism of the arylation can be depicted by the following scheme:



It should be mentioned that in our investigations it was the aryl sulfonates capable of being hydrolyzed by water that exhibited arylating properties [2]; for this reason it seemed to us that arylation and neutral hydrolysis in the case of the dinitro derivatives of aryl sulfonates both proceed by the aryl-oxygen mechanism. However, a study of the mechanism of the neutral and alkaline hydrolysis of dinitrophenyl benzenesulfonates with water containing heavy oxygen revealed that in both cases the hydrolysis is accomplished by the acyl-oxygen mechanism [3].

As a result, if in the case of alkyl sulfonates both alkylation and hydrolysis proceed by the alkyl-oxygen mechanism [4-8], then in the case of aryl sulfonates the arylation and hydrolysis are accompanied by a rupture of different reaction linkages (the aryl-oxygen linkage in the case of arylation, and the acyl-oxygen bond in the case of hydrolysis).

The intermediate stages of both processes are also different. If hydrolysis of the dinitro derivatives of aryl sulfonates is accomplished as the result of nucleophilic attack of the OH^- ion on the sulfur atom [3], then in the reaction of dinitro derivatives of aryl sulfonates with amines the formation of intermediate quinoid forms apparently precedes rupture of the aryl-oxygen bond. The transesterification reactions of dinitrophenol esters, for which the intermediate formation of quinoid forms has been shown [9], can serve as indirect evidence of this.

We were unable to isolate the intermediate compounds, but it is highly probable that if strongly activated compounds form intermediate complexes in substitution reactions, which can be isolated, then less activated compounds should also form similar compounds, but not sufficiently stable to permit their isolation.

EXPERIMENTAL

The reaction of aryl sulfonates with amines was run in 90% alcohol. Because of the great volatility of methylamine, dimethylamine and ethylamine we used their salts. The dry alkali was sifted into a Wurtz flask, and then a saturated water solution of the amine hydrochloride was added from a dropping funnel in drops. Gaseous ammonia was passed for 20 min into a 90% alcohol-water solution containing the dinitrophenyl benzenesulfonate. The reaction flask was cooled to 0°. At the end of reaction the temperature was gradually raised to room temperature and kept at this temperature for another 30 min. In the case of diethylamine and isopropylamine the synthesis was accomplished by heating the indicated amines with the alcohol-water solution of the ester in an ampul at 70° for 1 hour. The amine and ester were taken in a 2 : 1 ratio. Reaction with butylamine and with benzylamine was run in aqueous alcohol medium in a flask fitted with a reflux condenser, with heating for 30 min at 70°. On conclusion of reaction the alcohol was distilled off; at times a precipitate deposited, but more frequently an oil remained, which gave a precipitate when washed with dilute HCl solution. Depending on the place of bond rupture in the aryl sulfonates, the formation of the following reaction products could be expected: $C_6H_5SO_2NHR$ (I) and $C_6H_5(NO_2)_2OH$ (II) in the case of acyl-oxygen fission, and $(NO_2)_2C_6H_3NHR$ (III) and $C_6H_5SO_2OH \cdot RNH_2$ (IV) in the case of the aryl-oxygen mechanism. The obtained precipitate was washed with water. Compounds (I-III) could be on the filter, while the amine salt remained in the water solution, from which it was isolated by evaporation of the latter. The precipitate on the filter was heated with dilute NaOH solution, where substance (II), and at times also (I), went into solution, while the alkylaryl amines remained on the filter. The aqueous alkaline solution was shaken with ether to extract any alkylarylamine that might have gone into solution during the heating. The ether was evaporated, and the precipitates were combined and then recrystallized from alcohol to give the alkylaryl amines as yellow products. The aqueous alkaline solution after ether extraction was acidified and again extracted with ether. The ether was distilled off, and the precipitates were combined. Compounds (I) and (II) were separated by heating the mixture with water, where (I) hardly dissolved, while (II) went into solution and deposited again on cooling.

The synthesis of 2,4-dinitro-N,N-dimethylaniline is presented as an example. A solution of 1.62 g of 2,4-dinitrophenyl benzenesulfonate in 25 ml of 90% alcohol was cooled in ice and then a steady stream of gaseous dimethylamine was passed into it. The order of running the experiment and isolation of the reaction products was analogous to that described above. After recrystallization from alcohol we obtained 0.6 g (57%) of yellow crystals of 2,4-dinitro-N,N-dimethylaniline, while from the aqueous solution we obtained 0.636 g (63%) of the dimethylamine salt of benzenesulfonic acid. We isolated 0.303 g (33%) of 2,4-dinitrophenol from the aqueous alkaline solution. Recrystallization from alcohol gave us 0.138 g (15%) of N,N-dimethylbenzenesulfonamide. Subsequently we isolated only the alkylaryl amines and the dinitrophenol, and judged the direction of the reaction from their yield. The results of the experiments are given in the Table.

Reaction of 2,4-Dinitrophenyl Benzenesulfonate With Aliphatic Amines

Reagent	Reaction product $R = 2,4-(NO_2)_2C_6H_3$	Yield (in %)	Melting point
CH_3NH_2	$RNHCH_3$	10	171-173°
$(CH_3)_2NH$	$RN(CH_3)_2$	57	86-87
$C_2H_5NH_2$	$RNHCH_2CH_3$	25	113-114
$(C_2H_5)_2NH$ *	$RN(C_2H_5)_2$	60	78-80
$C_3H_7NH_2$	$RNHCH_2CH_2CH_3$	55	91-92
$(CH_3)_2CHNH_2$ *	$RNHCH(CH_3)_2$	70	94-95
$C_4H_9NH_2$	$RNHCH_2CH_2CH_2CH_3$	70	89-90
$C_6H_5CH_2NH_2$	$RNHCH_2C_6H_5$	90	115-116

* Synthesis carried out in ampuls.

The results of the experiments show that the yields of the alkylaryl amines are much lower than of the diarylamines [1], which is probably due to the greater volatility of aliphatic amines. When the reaction is run in ampuls the yield in the case of the dinitrodiethylaniline reaches 60% instead of 47%, while in the case of benzylamine it reaches 90%. In the case of butylamine, running the reaction at room temperature for 5 hr causes the yield to increase to 90%.

SUMMARY

1. A study was made of the reaction of 2,4-dinitrophenyl benzenesulfonate with the aliphatic amines—methylamine, ethylamine, diethylamine, isopropylamine, benzylamine, butylamine, and piperidine. In all cases we were able to isolate the corresponding alkylarylamines; depending on the nature of the starting amine, their yield ranged from 10 to 90%.

2. It can be considered established that the reaction of 2,4-dinitrophenyl benzenesulfonate with both aliphatic and aromatic amines is accomplished by the aryl-oxygen mechanism.

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REACTIONS OF ESTERS OF AROMATIC SULFONIC ACIDS

X. REACTION OF DINITRO-SUBSTITUTED ARYL SULFONATES

WITH ANILINE AND OTHER NUCLEOPHILIC REAGENTS

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A study of the mechanism of the hydrolysis of aryl sulfonates employing kinetic and isotopic methods reliably indicates that bond fission takes place between the acyl radical and oxygen [1-4]. It could be expected that also in other nucleophilic substitution reactions the dinitro-substituted aryl sulfonates should react by the acyl-oxygen mechanism (similar to the situation that prevails in the case of alkyl sulfonates). However, diaryl- and arylalkylamines were obtained when dinitro-substituted aryl sulfonates were reacted with aromatic and aliphatic amines, which indicated that these reactions went by the aryl-oxygen mechanism [5].

In order to elucidate the mechanism of the arylation reaction, and also because of the importance of the practical utilization of the arylation properties of aryl sulfonates, it was interesting to ascertain the influence of the structural traits of aryl sulfonates on the yield of arylation products and the effect of the nature of the nucleophilic reagent on the fission of the acyl-oxygen or the aryl-oxygen bond.

For this we investigated the reaction of the dinitro- and nitro-substituted phenyl benzenesulfonates with aniline, and also the reaction of 2,4-dinitrophenyl benzenesulfonate with various nucleophilic reagents, and specifically, with hydrogen sulfide, potassium hydrosulfide, sodium sulfide, hydrazine, phenylhydrazine, sodium thiophenolate, sodium p-nitrothiophenolate, and sodium phenolate.

Analysis of the experimental data presented in Table 1 indicates that an important difference exists in the influence exerted by the nature and position of substituents in the benzenesulfonic acid and in the phenol on the arylation properties of aryl sulfonates.

If the introduction of the chlorine atom in the p-position of the benzenesulfonic acid or of methyl groups in the o- and p-positions fails to affect the yield of arylation products, then an imperative condition for fission of the aryl-oxygen bond is the presence in the phenol of nitro groups in the o- or the o-, p-positions to the carbon atom attached to the ether oxygen. The absence of a steric effect by o-substituents indicates that the attacking reagent approaches perpendicularly to the plane of the ring, and for this reason substitution in the aromatic series is quite insensitive to the size of the substituent in the o-position.

A comparison of the results obtained by us with the data existing in the literature [6-9] makes it possible to express, with a high degree of probability, the theory that also in our experiments the arylation reaction proceeds via the intermediate formation of quinoid forms in accordance with the scheme:

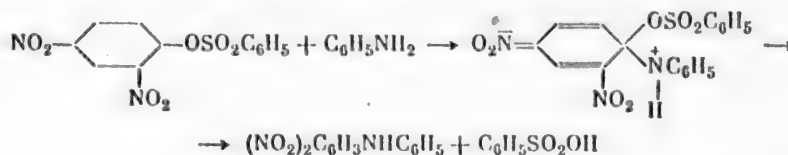


TABLE 1

Reaction of Dinitrophenyl Benzenesulfonates With Aniline

Reagent	Reaction products, R = C ₆ H ₅	Yield (in %)	Melting point
C ₆ H ₅ SO ₂ OC ₆ H ₃ (NO ₂) ₂ -2,4	RNHC ₆ H ₃ (NO ₂) ₂ -2,4	90	155—156°
C ₆ H ₅ SO ₂ OC ₆ H ₃ (NO ₂) ₂ -2,6	RNHC ₆ H ₃ (NO ₂) ₂ -2,6	80	105—106
4-ClC ₆ H ₃ SO ₂ OC ₆ H ₃ (NO ₂) ₂ -2,5 *	RNHC ₆ H ₃ (NO ₂) ₂ -2,5	20	83—90
4-ClC ₆ H ₃ SO ₂ OC ₆ H ₃ (NO ₂) ₂ -3,4	Red oil	—	—
4-ClC ₆ H ₃ SO ₂ OC ₆ H ₃ -2NO ₂ -4Cl	RNHC ₆ H ₃ -2NO ₂ -4Cl	Traces	59—61
4-ClC ₆ H ₃ SO ₂ OC ₆ H ₃ -2Cl-3NO ₂	No reaction	—	—
4-ClC ₆ H ₃ SO ₂ OC ₆ H ₃ -2Cl-4NO ₂	No reaction	—	—
Sym. (CH ₃) ₂ C ₆ H ₃ SO ₂ OC ₆ H ₃ (NO ₂) ₂ -2,4	RNHC ₆ H ₃ (NO ₂) ₂ -2,4	86	155—156
Sym. (CH ₃) ₂ C ₆ H ₃ SO ₂ OC ₆ H ₃ (NO ₂) ₂ -2,6	RNHC ₆ H ₃ (NO ₂) ₂ -2,6	75	105—106

TABLE 2

Reaction of 2,4-Dinitrophenyl Benzenesulfonate With Nucleophilic Reagents

Reagent	Reaction product R = 2,4-(NO ₂) ₂ C ₆ H ₃	Yield (in %)	Melting point
p-NO C ₆ H ₄ SNa	RSC ₆ H ₄ NO ₂ -p	81	159—160°
C ₆ H ₅ Na	RSC ₆ H ₅	90	120—121
	RSH	15	130—131
	R-S-S-R	50	Doesn't melt at 250°
KSH	R-S-S-R	55	Doesn't melt at 250°
Na ₂ S	R ₂ S	70	190—191
C ₆ H ₅ NH ₂ **	RNHC ₆ H ₅	90	155—156
NH ₂ -NH ₂	RNHNH ₂	40	193—194
C ₆ H ₅ NHNH ₂	Red tar	—	—
H ₂ O **	ROH	95	113—115
KOH **	ROH	95	113—115
C ₆ H ₅ ONa	ROH	90	113—115

The results given in Table 2 indicate that two reactive sites are present in aryl sulfonates, the sulfur of the sulfonyl group and the carbon of the benzene ring, the electron density of which is decreased due to the joint effect of the NO₂ group and the negative induction effect of the oxygen atom, as a result of which reaction with amines and such nucleophilic reagents as H₂S, KSH, Na₂S, C₆H₅SNa, etc. is accomplished quite easily and proceeds by the aryl-oxygen mechanism. However, nucleophilic attack by such reagents as KOH, H₂O and C₆H₅ONa is directed toward the sulfur of the sulfonyl group, and in this case the reaction proceeds by the acyl-oxygen mechanism. The latter also shows not too clearly that in this case a strict parallelism fails to exist between nucleophilicity and basicity, and it is quite possible that the mechanism of the reaction also depends on the atomic radii and the polarizability of the atoms.

EXPERIMENTAL

We studied the reaction of aniline with 2,4-dinitro- and 2,6-dinitrophenyl benzenesulfonates, phenyl mesitylenesulfonates, 2,5-dinitro- and 3,4-dinitro-4-chlorophenyl benzenesulfonates, and also with the nitro-chlorophenyl 4-chlorobenzenesulfonates, containing the 2NO₂-4Cl, 2Cl-4NO₂, and 2Cl-3NO₂ groups. The melting points and the yields are given in Table 1. The data on the reaction of 2,4-dinitrophenyl benzene-sulfonate with various nucleophilic reagents is summarized in Table 2. The reacting ester (0.0033 mole) and aniline were taken in a 1:2 ratio. The reactant mixture was dissolved in 25 ml of 90% alcohol and then heated on the water bath. The solution turned red, and by the end of reaction had become almost cherry-red

* Reaction is slow, and the mixture was heated for 3 hr.

** The data on the aqueous and alkaline hydrolysis were taken from [3], while the data on the reaction with aniline was taken from [5].

in color. At the end of reaction, half of the alcohol was distilled off. The residue on cooling deposited cherry-red precipitates of the dinitrodiphenylamines. A more detailed description of the synthesis procedure and isolation of the reaction products is given in an earlier paper [5]. When the aryl sulfonates were reacted with aniline we isolated only the diphenylamines and judged the direction of the reaction by their yields.

Reaction with p-nitrothiophenol. This reaction was run in alcohol. To obtain the salt, the calculated amount of KOH was added to an alcohol solution of the phenol (the solution became cherry-red). The ester (1.08 g) was dissolved separately in alcohol. The two warm solutions were poured together, the red color disappeared, and the solution on standing for 40 min (at 30°) deposited a yellow precipitate. The reactants were taken in a 1 : 2 ratio. The obtained precipitate was washed with water, and then recrystallized from glacial acetic acid. The yield of 2,4,4-trinitrodiphenyl sulfide was 81%. Replacing the 90% alcohol by 70% dioxane-water solution failed to reduce the yield of reaction products.

Reaction with thiophenolate. The reaction was run the same as in the case of the p-nitrothiophenolate. The appearance of a red color was not observed in this case. Yellow crystals of 2,4-dinitrodiphenyl sulfide were isolated.

Reaction with H₂S. Hydrogen sulfide was bubbled for 3 hr into a solution of 1.08 g of the ester in 70% aqueous dioxane. The colorless solution gradually assumed a yellow-orange color, and a yellow precipitate deposited. The precipitate was filtered and washed. It did not melt at 250°. Analysis for sulfur and nitrogen corresponded to the tetranitrodiphenyl disulfide. The solvent was distilled from the filtrate and acidification of the residue gave 0.1 g of the dinitrothiophenol.

Reaction with KSH. An alcohol solution of 2,4-dinitrophenyl benzenesulfonate (1.08 g) was mixed with an alcohol solution of freshly prepared KSH solution. The solution turned red and was allowed to stand at 40° for 60 min. Then the alcohol was vacuum-distilled, while the residue was washed with water and then acidified; here a yellow precipitate deposited, which was purified by reprecipitation with caustic. The yellow precipitate did not melt when heated to 250°, and above this temperature it decomposed with explosive violence. The analysis for sulfur and nitrogen corresponded to the tetranitrodiphenyl disulfide.

Reaction with Na₂S. This reaction was run both in 90% alcohol and in 70% aqueous dioxane, the same as in the case of the KSH. The solution turned red at the start, and then a yellow precipitate deposited, which proved to be insoluble in alcohol, water, and alkali. After recrystallization from glacial acetic acid, m. p. 191°. The reactants were taken in a 2 : 1 ratio. Unreacted ester could not be detected. However, we did isolate traces of 2,4-dinitrophenol and 0.850 g of the tetranitrodiphenyl sulfide.

Reaction with hydrazine. An alcohol solution of the ester (1.08 g) was heated on the water bath with a freshly prepared alcohol solution of hydrazine hydrate. The solution turned red, and after 10-20 min a red precipitate deposited, which was filtered, washed with water, and then recrystallized several times. The yield of 2,4-dinitrophenylhydrazine was 40%. A red tar was obtained when the reaction was run with phenylhydrazine.

Reaction with sodium phenolate. The reaction was run in 90% aqueous alcohol solution and was repeated in absolute alcohol. The alcohol solution of the reactants was heated on the water bath for 20 min. The reactants were taken in a 1 : 1 ratio. The alcohol was distilled off, while the residue was diluted with water and then acidified; the solution on standing deposited a precipitate of the dinitrophenol and oil, the latter corresponding to phenyl benzenesulfonate. In this case the arylation reaction failed to take place, and instead transesterification occurred.

SUMMARY

1. A study was made of the reaction of dinitro- and nitrochloro-substituted phenyl benzenesulfonates, having the substituents in different positions, with aniline, and the corresponding dinitrodiarylamines were isolated.

2. A study was made of the reaction of 2,4-dinitrophenyl benzenesulfonate with p-NO₂C₆H₄SNa, C₆H₅SNa, H₂S, KSH, Na₂S, NH₂-NH₂ and C₆H₅ONa, and here we isolated the trinitrodiphenyl sulfide, dinitrodiphenyl sulfide, tetranitrodiphenyl disulfide, tetranitrodiphenyl sulfide, 2,4-dinitrophenylhydrazine and 2,4-dinitrophenol, respectively.

3. It was established that in all of the examined reactions, with the exception of sodium phenolate, and also in neutral and alkaline hydrolysis, reaction of dinitro-substituted aryl sulfonates with nucleophilic reagents is accomplished by the aryl-oxygen mechanism.

4. It was established that arylating properties are manifested by those aryl sulfonates that contain o-nitro or o-, p-dinitro groups relative to the ether oxygen.

5. The theory was expressed that arylation is accomplished via the intermediate formation of quinoid forms.

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1,1,3,3,-TETRAFLUOROPHTHALAN AND ITS DERIVATIVES

L. M. Yagupol'skii

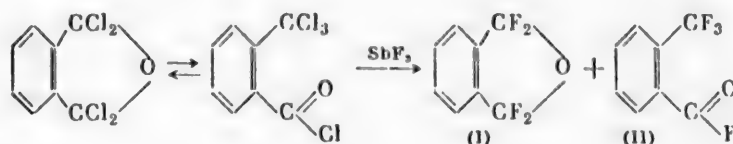
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It is known that symmetrical phthaloyl chlorides and bromides and asymmetrical dichloro- and dibromo-phthalides are capable of interconversion into each other [1, 2]. Analogous rearrangements are observed in the case of 1,1,3,3-tetrachlorophthalan and *o*-trichloromethylbenzoyl chloride [3]. In contrast to this, the symmetrical phthaloyl fluoride is not isomerized to the difluorophthalide [4, 5]. It was interesting to determine if 1,1,3,3-tetrafluorophthalan and *o*-trifluoromethylbenzoyl fluoride are capable of mutual interconversion. Both of these compounds are new.

We decided to prepare 1,1,3,3-tetrafluorophthalan from 1,1,3,3-tetrachlorophthalan using antimony trifluoride. However, here we obtained a mixture of two compounds, namely 1,1,3,3-tetrafluorophthalan (I) and *o*-trifluoromethylbenzoyl fluoride (II).



Fluoride (II) was converted to the amide by passing ammonia into a petroleum ether solution of the obtained mixture of (I) and (II). The amide was separated by filtration, while the 1,1,3,3-tetrafluorophthalan was isolated by distillation. The latter was obtained as a colorless liquid with b. p. 153°.

It was interesting to determine the manner in which fluoride (II) is formed in the fluorination of 1,1,3,3-tetrachlorophthalan, whether by isomerization of the 1,1,3,3-tetrafluorophthalan or because of the easy isomerization of 1,1,3,3-tetrachlorophthalan under the influence of heat to *o*-trichloromethylbenzoyl chloride and its subsequent fluorination. Apparently, the second postulation is the correct one. 1,1,3,3-Tetrafluorophthalan is stable to heat. It does not change when heated in a glass ampul for 24 hr at 200° (the refractive index remains the same, and the passage of ammonia fails to yield the amide). The fluorination of *o*-trichloromethylbenzoyl chloride with antimony trifluoride also yields a mixture of *o*-trifluoromethylbenzoyl fluoride and 1,1,3,3-tetrafluorophthalan. Apparently, also in this case the heating of *o*-trichloromethylbenzoyl chloride causes its partial isomerization to 1,1,3,3-tetrachlorophthalan, and then each isomer is fluorinated separately. The isolation of *o*-trifluoromethylbenzoyl fluoride from its mixture with 1,1,3,3-tetrafluorophthalan is difficult, and consequently the compound was obtained by the fluorination of *o*-trifluoromethylbenzoyl chloride using antimony trifluoride; 1,1,3,3-tetrafluorophthalan is not formed here.

As a result, fluoride (II) is not converted to tetrafluorophthalan (I) in the presence of either antimony trifluoride or trichloride. Even when *o*-trifluoromethylbenzoyl fluoride is heated in a stainless steel autoclave for 10 hr at 200° it is not converted to 1,1,3,3-tetrafluorophthalan, as shown by the fact that fluoride (II) after such heating gives the amide of *o*-trifluoromethylbenzoic acid in quantitative yield when treated with ammonia.

The absorption spectrum of 1,1,3,3-tetrafluorophthalan (the absorption maxima lie at 242, 246, 252, 257, and 263 $m\mu$) resembles the absorption spectrum of 1,1,3,3-tetrachlorophthalan (absorption maxima at 220, 247, 252, 258, 264, and 269 $m\mu$) and is quite different from the absorption spectrum of *o*-trifluoromethylbenzoyl fluoride (absorption maxima at 226 and 274 $m\mu$). The absorption curves of the indicated compounds are shown in Fig. 1.

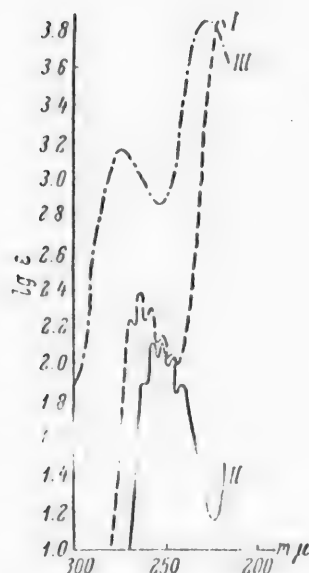


Fig. 1. Absorption spectra. I) 1,1,3,3-Tetrachloro - phthalan; II) 1,1,3,3-tetrafluorophthalan; III) *o*-tri-fluoromethylbenzoyl fluo-ride

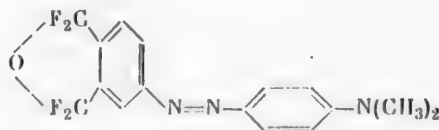
1,1,3,3-Tetrafluorophthalan is stable toward alkaline agents. It remains unchanged when heated with an alcoholic solution of diethylamine at 150° for 3 hr. Concentrated acids decompose it only when heated.

We were unable to obtain the nitrotetrafluorophthalan when 1,1,3,3-tetrafluorophthalan was nitrated with mixed acid. Hydrogen fluoride began to be evolved even at 40°. The nitration does not go at lower temperatures; consequently, to obtain the nitrotetrafluorophthalan we started with 6-nitrophthalide. It is interesting that the reaction of the latter with phosphorus pentachloride gave only the cyclic 5-nitro-1,1,3,3-tetrachlorophthalan. The presence of nitro-*o*-trichloromethylbenzoyl chloride could be detected. The mixing of benzene solutions of aniline and the reaction product of 6-nitrophthalide with phosphorus pentachloride failed to yield the anilide even when the mixture was allowed to stand for a day.

The fluorination of 5-nitro-1,1,3,3-tetrachlorophthalan using antimony trifluoride gave 5-nitro-1,1,3,3-tetrafluorophthalan. The absorption spectra of 5-nitro-1,1,3,3-tetrachlorophthalan (absorption maxima at 219, 242, 247, 252, 258, and 264 $m\mu$) and 5-nitro-1,1,3,3-tetrafluorophthalan (absorption maxima at 236, 241, 246, 252, 258, and 265 $m\mu$) (Fig. 2) resemble the absorption spectra of the 1,1,3,3-tetrachloro- and tetrafluorophthalans.

5-Nitro-1,1,3,3-tetrafluorophthalan was reduced to the amino compound. 5-Amino-1,1,3,3-tetrafluorophthalan is an unstable compound and decomposes on storage. Its acetyl derivative is completely stable. Employing the Sandmeyer reaction, this amine was converted to the cyano derivative, which was hydrolyzed to 5-carboxy-1,1,3,3-tetrafluorophthalan by refluxing with aqueous caustic, and was converted to 5-fluoro-1,1,3,3-tetrafluorophthalan by the Schiemann reaction. The absorption maxima of this compound (246, 253, 259, 264, and 269 $m\mu$)* are shifted somewhat toward longer wavelengths when compared with 1,1,3,3-tetrafluorophthalan (Fig. 3).

When the diazonium salt from 6-amino-1,1,3,3-tetrafluorophthalan was coupled with dimethylaniline we obtained the azo dye,



λ_{\max} (in alcohol solution) 450 $m\mu$, $\epsilon \cdot 10^{-4}$ 3.15; in acid solution (2 volumes of alcohol and 1 volume of hydrochloric acid, d 1.19), λ_{\max} 496 $m\mu$, and $\epsilon \cdot 10^{-4}$ 4.28. The effect exerted by the $\text{O} \begin{smallmatrix} \text{CF}_3 \\ \diagup \\ \text{CF}_3 \end{smallmatrix}$ grouping on the color of *p*-dimethylaminoazo dyes resembles that of strong electronegative substituents [6].

EXPERIMENTAL

1,1,3,3-Tetrafluorophthalan. A charge of 20 g of 1,1,3,3-tetrachlorophthalan** and 20 g of SbF_3 was placed in a Claisen flask, the mixture heated with a free flame, followed by distillation of the reaction products under the slight vacuum of a water-jet pump, and the distillate was dissolved in a mixture of light petroleum

*All of the absorption curves were taken in *n*-hexane.

**M. p. 85–86° [3].

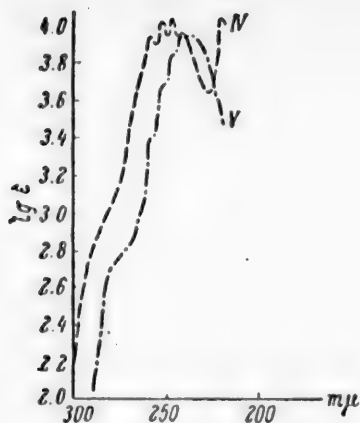


Fig. 2. Absorption spectra. IV) 5-Nitro-1,1,3,3-tetrachlorophthalan; V) 5-nitro-1,1,3,3-tetrafluorophthalan.

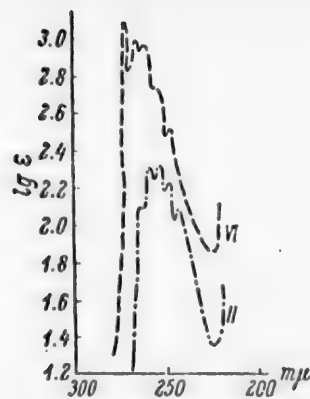


Fig. 3. Absorption spectra. II) 1,1,3,3-Tetrafluorophthalan; VI) 5-fluoro-1,1,3,3-tetrafluorophthalan.

ether and 20% hydrochloric acid. The petroleum ether layer was separated, and then washed in sequence with hydrochloric acid and water. The product was dried over sodium sulfate. Then dry ammonia was passed into the solution of the product. The amide of *o*-trifluoromethylbenzoic acid was filtered, washed with water, and then recrystallized from aqueous alcohol. The yield was 2.95 g (20%). M. p. 160° [7]. The filtrate was distilled to remove the petroleum ether, and then the 1,1,3,3-tetrafluorophthalan was isolated by distillation. Yield 8.5 g (57.4%).

B. p. 153°, n_D^{20} 1.4155, d_4^{20} 1.387, MR_D 34.72; calc. 34.57.

Found %: C 50.01, 50.04; H 2.12, 2.14. $C_8H_4OF_2$. Calculated %: C 50.00; H 2.08.

***o*-Trifluoromethylbenzoyl fluoride.** A mixture of 5 g of *o*-trifluoromethylbenzoyl chloride (obtained from *o*-trifluoromethylbenzoic acid [7] and thionyl chloride; b. p. 199° or 91–92° at 18 mm) and 2 g of antimony trifluoride was heated with a free flame, and the liquid with b. p. 171–180° was distilled off. This liquid was dissolved in petroleum ether, and the solution was washed first with hydrochloric acid and then with water, dried, and distilled. Yield 3 g (65.2%).

B. p. 175–176°; n_D^{22} 1.4411, d_4^{26} 1.396.

Found %: C 50.33, 50.41; H 1.99, 2.05. $C_8H_4OF_4$. Calculated %: C 50.00; H 2.08.

5-Nitro-1,1,3,3-tetrachlorophthalan. A mixture of 3.6 g of 6-nitrophthalide [8], 12.4 g of phosphorus pentachloride and 1 ml of phosphorus oxychloride in a Claisen flask was heated in a glycerin bath for 30 min at 110°, and then it was refluxed for 1 hour until the hydrogen chloride ceased to evolve. The phosphorus trichloride and phosphorus oxychloride were vacuum-distilled using a water-jet pump. The residue was recrystallized from benzene. Yield 4.9 g (75.5%). M. p. 82–83°.

Found %: Cl 46.92, 47.00. $C_8H_3O_3NCl_4$. Calculated %: Cl 46.86.

5-Nitro-1,1,3,3-tetrafluorophthalan. The 5-nitro-1,1,3,3-tetrachlorophthalan obtained in the previous experiment (without purification) was treated with 6 g of antimony trifluoride. The mixture was heated with a free flame, and then it was distilled using the vacuum of a water-jet pump. The product was dissolved in ether and then washed with 20% hydrochloric acid. The ether was distilled off. Yield of product 2 g (42.3%), based on the starting 6-nitrophthalide. M. p. 57–58° (from aqueous alcohol).

Found %: N 5.74, 5.89. $C_8H_3O_3NF_4$. Calculated %: N 5.90.

5-Amino-1,1,3,3-tetrafluorophthalan. A solution of 2 g of 5-nitro-1,1,3,3-tetrafluorophthalan in 15 ml of alcohol was reduced with hydrogen using platinum catalyst. The alcohol was distilled off. The yield of product was quantitative (1.75 g).

B. p. 87–88° (2 mm), n_D^{16} 1.4778, d_4^{16} 1.539, MR_D 38.16; calc. 37.91.

5-Nitro-1,1,3,3-tetrafluorophthalan can also be reduced to the amine using stannous chloride. Yield 75%.

Found %: N 6.72, 6.75. $C_8H_5ONF_4$. Calculated %: N 6.76.

Acetyl derivative, m. p. 139–140°, from aqueous alcohol.

Found %: N 5.43, 5.54. $C_{10}H_7O_2NF_4$. Calculated %: N 5.62.

5-(4-dimethylaminophenylazo)-1,1,3,3-tetrafluorophthalan. A solution of 1 g of 5-amino-1,1,3,3-tetrafluorophthalan in 4 ml of hydrochloric acid (d 1.19) and 16 ml of water was diazotized with 0.35 g of sodium nitrite and then coupled with a solution of 0.6 g of dimethylaniline in 4 ml of acetic acid. Yield 1 g (59%). M. p. 120–121°, from methyl alcohol.

Found %: N 12.18, 12.25. $C_{16}H_{13}ON_3F_4$. Calculated %: N 12.38.

5-Cyano-1,1,3,3-tetrafluorophthalan. A mixture of 5 g of the 5-aminotetrafluorophthalan and 12 ml of hydrochloric acid (d 1.19) was diazotized with a solution of 1.7 g of sodium nitrite in 5 ml of water at 0°. The diazo solution was filtered, then neutralized with sodium acetate and added with cooling to a solution of cuprous cyanide, prepared from 2.3 g of cuprous chloride, 6 g of sodium cyanide and 12 ml of water. The next day the mixture was heated to 60°. The product was steam-distilled and then recrystallized from alcohol. Yield 3.5 g (67.3%). M. p. 75–76°.

Found %: N 6.32, 6.35. $C_9H_3ONF_4$. Calculated %: N 6.45.

1,1,3,3-Tetrafluoro-5-phthalanecarboxylic acid. A mixture of 2.17 g of the nitrile and 5 ml of 10% NaOH solution was heated under reflux until ammonia evolution ceased. Then the solution was acidified. The obtained precipitate was filtered and recrystallized from alcohol. Yield 2 g (84.7%). M. p. 176–177°.

Found %: F 32.11, 32.36. $C_9H_4O_3F_4$. Calculated %: F 32.22.

5-Fluoro-1,1,3,3-tetrafluorophthalan. A mixture of 5.2 g of the 5-aminotetrafluorophthalan and 12 ml of concd. hydrochloric acid was diazotized with a solution of 1.75 g of sodium nitrite in 5 ml of water at 0°. The diazo solution was filtered and then mixed with vigorous stirring with the fluoboric acid prepared from 3 g of boric acid and 9 g of 40% hydrofluoric acid. The diazonium fluoborate was filtered, washed with cold alcohol and then with ether, and dried. M. p. 150° (with decompn.). The compound was decomposed by heating with a free flame and the product was distilled off. Yield 3.5 g (67.3%).

B. p. 141–142°, n_D^{20} 1.4042, d_4^{20} 1.481, M_R 34.67; calc. 34.47.

Found %: C 46.09, 46.16; H 1.46, 1.49. $C_8H_3OF_5$. Calculated %: C 45.71; H 1.43.

SUMMARY

The synthesis of 1,1,3,3-tetrafluorophthalan and its 5-nitro, 5-amino, 5-cyano, 5-carboxy and 5-fluoro derivatives was described. It was shown that 1,1,3,3-tetrafluorophthalan and *o*-trifluoromethylbenzoyl fluoride, in contrast to the corresponding chloro derivatives, do not isomerize to each other when heated.

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* Original Russian pagination. See C. B. translation.

SYNTHESIS AND TRANSFORMATIONS IN THE DIARYLUREA SERIES

XIV. SOME PROBLEMS OF THE PHYSICAL STATE OF DIARYLUREAS

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As we had shown [1-3], diarylureas are highly resistant to hydrolysis. Together with this, they are capable of certain chemical transformations. It is characteristic that the differences in the chemical properties of individual members of the diarylurea series are trivial, and, in addition, are observed only under drastic conditions. Starting with the structures of the investigated compounds, we attempted to find an explanation for this characteristic.

In order to study the effect of the number of substituents in the phenyl rings and their nature on the valence vibrations of the carbonyl group we investigated the infrared spectra of a number of diarylureas. Here we obtained the results presented in Table 1.

As can be seen from the data in Table 1, the valence vibration frequencies of the carbonyl groups in diarylureas are basically the same for all of the compounds. The introduction of substituents, irrespective of the number or their nature, into the aromatic rings of diarylureas is practically without effect on the valence vibrations of the carbonyl group. In this case the induction effect, for example, of chlorine atoms found in the aromatic rings of diarylureas, is not in a position to change the value of the vibration frequencies of the carbonyl group.

Apparently, this phenomenon can be explained by the fact that the carbonyl group displays a well-defined tendency to enter into hydrogen bonding of the type $>C=O \cdots H-N<$ [4]. It must be assumed that the effect of the hydrogen bond is stronger than the induction effect through the ring, which leads to the influence of the hydrogen bond on the $C=O$ frequency prevailing over the corresponding influence of substituents in the ring. Starting with these concepts, it becomes possible to explain the constancy of the frequencies of the $C=O$ bond in the case of nuclear chloro derivatives of diarylureas and unsubstituted diphenylurea.

As a result, the peculiar chemical properties shown by diarylureas can apparently be explained by the presence of hydrogen bonds between the oxygen of the carbonyl group and the hydrogens attached to the nitrogen atoms of the diarylureas. Starting with this assumption makes it possible to explain some decrease in the basic properties of the diarylureas—a suppression of the activity of the double bond of the carbonyl group and in that way an increase in the chemical stability.

Replacing the hydrogen atoms attached to the nitrogen atoms in diarylureas by chlorine sharply changes the physical state of diarylureas. We studied the infrared absorption spectra of various N-chloro diarylurea derivatives and determined the valence vibration frequencies of the carbonyl groups in these compounds. Here we obtained the results given in Table 2.

From the results given in Table 2 it can be seen that a completely different picture prevails here. If the valence vibration frequencies of the carbonyl bond in the starting diarylureas were basically the same and corresponded to a value of 1640 cm^{-1} , then for the N-chloro diarylurea derivatives the valence vibration frequencies of the $C=O$ bond are different, and even the minimum value is 1709 cm^{-1} . Then, in addition, there is an increase in the valence vibration frequencies of the $C=O$ bond with increase in the number of halogens in the

TABLE 1

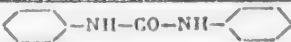
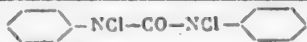
Substituents in 	λ_{\max} (in cm^{-1})
Unsubstituted diphenylurea	1640
2,4,2',4'-Tetrachloro-	1640
2,4,6,2',4',6'-Hexachloro-	1640
2,3,5,6,2',3',5',6'-Octachloro-	1640
2,4,6,2',4'-Pentachloro-	1643
2,4,6,4'-Tetrachloro-	1645
2,4,5,2',4',5'-Hexafluoro-	1646 and 1683

TABLE 2

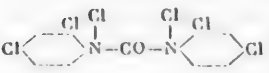
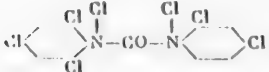
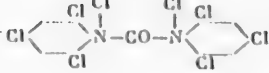
Substituents in 	λ_{\max} (in cm^{-1})
2,4,2',4'-Tetrachloro- (I)	1709
2,6,2',6'-Tetrachloro-	1714
2,4,6,2',4',6'-Hexachloro- (III)	1721
2,4,5,2',4',5'-Hexachloro-	1723
2,3,5,6,2',3',5',6'-Octachloro-	1735
2,4,5,2',4',5'-Hexafluoro-	1727
2,4,6,2',4'-Pentachloro- (II)	1730

aryl radicals of the N-chloro diarylurea derivatives. Apparently, this fact also indicates that hydrogen bonds are present in the starting diarylureas.

The values observed for the vibration frequencies of the carbonyl group in N-chloro diarylurea derivatives are found in agreement with the concepts being developed at the present time regarding the induction effect of substituents on the vibration frequencies of the C=O bond [5, 6].

The increase established by us in the valence vibration frequencies of the carbonyl group in N-chloro diarylurea derivatives with increase in the number of substituents in their phenyl rings is in harmony with the change in the values of the dipole moments. We were the first to determine the dipole moments of a number of N-chloro diarylurea derivatives, and specifically: N,N'-dichloro-2,2',4,4'-tetrachlorodiphenylurea (I) 3.29 D, N,N'-dichloro-2,4,6,2',4'-pentachlorodiphenylurea (II) 3.45 D, and N,N'-dichloro-2,2',4,4',6,6'-hexachlorodiphenylurea (III) 3.88 D.

TABLE 3

Compound	f	ϵ^{25}	d_r^{25}	MR	P_{∞}	$\mu \cdot 10^{-18}$
	0.0008949	2.2865	0.87555		316.82	3.26
	0.001457	2.2911	0.87605	97.92	333.65	3.38
	0.001303	2.2924	0.87655	95.67	314.25	3.24
	Average			96.79	321.57	3.29
	0.000932	2.2885	0.87585		343.29	3.41
	0.001068	2.2913	0.87612	104.29	349.94	3.45
	0.00151	2.3002	0.87731	101.13	354.86	3.49
	Average			102.71	349.36	3.45
	0.0013437	2.3033	0.87697		433.62	3.91
	0.0014195	2.3056	0.87745	114.57	442.18	3.97
	0.0015950	2.3074	0.87797	116.70	409.96	3.77
	Average			115.63	428.53	3.83

Legend: f is the mole fraction of substance in benzene solution; ϵ^{25} is the dielectric permittability of the solution at 25°; P_{∞} is the polarization; μ is the dipole moment.

From the obtained data it can be seen that the dipole moments of N-chloro diarylurea derivatives increase with increase in the number of chlorine atoms in the aromatic radicals.

EXPERIMENTAL

A "Perkin-Elmer" spectrophotometer, Model 12B, was used to take the infrared absorption spectra. The compounds were investigated as nujol mulls, deposited on potassium chloride plates.

We used a dielectric, operating on the beat principle, to determine the dielectric constants of dilute benzene solutions of the compounds. To calculate the complete polarization we used the Hedestrand equation [7], and for the dipole moment we used the expression $\mu = 0.2196 \sqrt{P_{\infty} - M/R}$. The refractive index of the compounds was determined by the technique of dissolving them in dichloroethane [8]. To calculate the dipole moment we took the average of two determinations of the molecular refraction (Table 3).

SUMMARY

1. As a result of studying the infrared absorption spectra of a number of diarylureas the theory was expressed that hydrogen bonds are present in these compounds between the oxygen of the carbonyl group and the hydrogen atoms attached to the nitrogen.

2. The dipole moments of a number of N-chloro diarylurea derivatives were determined; here it was shown that the value of the dipole moment increases with increase in the number of chlorine atoms in the aryl radicals.

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CARBON-SUBSTITUTED DERIVATIVES OF CARBOHYDRATES
WITH HETEROCYCLIC AGLYCONS

II. REACTION OF 1,2-NAPHTHALENEDIAMINE WITH ALDONIC ACIDS*

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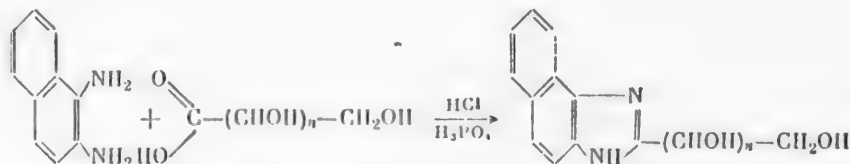
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Among carbon-carbon derivatives of carbohydrates with heterocyclic aglycons an important position is occupied by compounds in which the carbohydrate moiety is attached to the benzimidazole ring. The methods of preparation, the properties and the utilization of compounds of this type have been discussed in detail in review articles [1, 2].

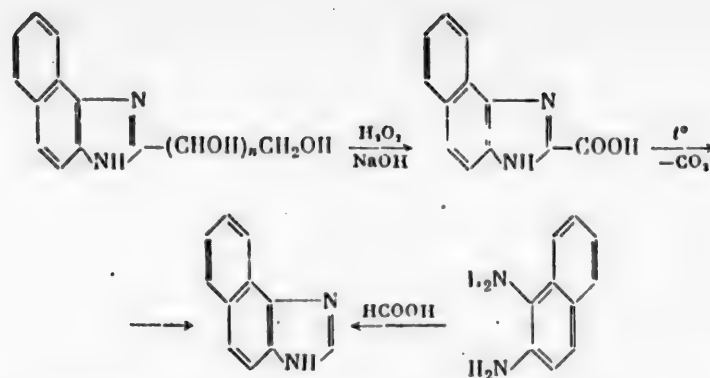
In our first communication [3] we described the synthesis of some benzimidazole derivatives that were obtained by the condensation of *o*-phenylenediamine with mono- and dibasic acids. The present paper is devoted to a study of the reaction of 1,2-naphthalenediamine with aldonic acids. Henseke and Lemke have shown that the condensation of 1,2-naphthalenediamine with D-glucosone yields a mixture of isomeric 2- and 3-(D-arabo-tetrahydroxybutyl)-5,6-benzoquinoxalines [4]. Condensation with the salts of aldonic acids (L-arabonic, D-xylonic, and D-galactonic) leads to the formation of 2-(aldo-polyhydroxyalkyl)-naphth [1, 2] imidazoles and proceeds by the following scheme:



The reaction was run by evaporating equimolar amounts of the components in aqueous alcohol solution at 135–140° in the presence of hydrochloric and orthophosphoric acids by the Moore and Link method [5]. 2-(Aldo-polyhydroxyalkyl)-naphth [1, 2] imidazoles are also obtained in good yield by refluxing the calcium salts of aldonic acids in 2N hydrochloric acid solution, by the method described for the synthesis of benzimidazole derivatives of carbohydrates [6].

The presence of the carbon-carbon linkage in the obtained compounds was shown by oxidation with alkaline hydrogen peroxide solution. Naphth [1, 2] imidazole-2-carboxylic acid was formed in the oxidation, which was decarboxylated to naphth [1, 2] imidazole, identical with the specimen obtained from 1,2-naphthalenediamine and formic acid [7].

*Communication I, see [3].



The obtained C-naphthimidazole carbohydrate derivatives are colorless compounds, readily soluble in dilute acids, but practically insoluble in water and the common organic solvents. From 2-(L-arabotetrahydroxybutyl)-naphth [1, 2] imidazole we prepared the picrate and the tetraacetyl derivative; 2-(D-galactopentahydroxyamyl)-naphth [1, 2] imidazole forms a hydrochloride that is readily soluble in water.

EXPERIMENTAL •

The aldonic acid calcium salts needed for the work were obtained by the oxidation of the aldoses with bromine water [8, 9]; 1,2-naphthalenediamine was obtained by the reduction of benzeneazo- β -naphthylamine with zinc dust in acetic acid [10].

2-(L-Arabotetrahydroxybutyl)-naphth [1, 2] imidazole. Method A. A mixture of 2.3 g (0.005 mole) of calcium arabonate pentahydrate, 1.58 g (0.01 mole) of 1,2-naphthalenediamine, 2 ml of water, 3 ml of alcohol, 3 ml of concd. hydrochloric acid and 1 ml of 85% orthophosphoric acid was held at 135–140° for 1.5 hr. The reddish-brown melt was dissolved in hot water, the solution was boiled with activated carbon, then filtered, and the filtrate was cooled and made alkaline with 10% ammonia solution. Here an amorphous precipitate deposited almost immediately, which was filtered, washed in sequence with water, alcohol and ether, and dried. The yield of compound was 1.8 g (62%). Recrystallization from 1.5 liters of water gave the compound as a colorless powder with m. p. 244–245 (decompn.).

Method B. A solution of 1.58 g of 1,2-naphthalenediamine and 2.3 g of calcium arabonate (pentahydrate) in 25 ml of 2N hydrochloric acid was refluxed for 5 hr. After boiling with activated carbon and making alkaline with ammonia we obtained 2 g of 2-(L-arabotetrahydroxybutyl)-naphth [1, 2] imidazole (69% yield). M. p. 244–245° (decompn.).

Found %: C 52.01, 52.09; H 5.49, 5.51; N 9.74, 9.83. $C_{15}H_{16}O_4N_2$. Calculated %: C 52.08; H 5.55; N 9.72.

The picrate of 2-(L-arabotetrahydroxybutyl)-naphth [1, 2] imidazole was obtained by boiling a water solution of the compound with picric acid. M. p. 211 (decompn.).

2-(L-Arabotetrahydroxybutyl)-naphth [1, 2] imidazole tetraacetate. To 0.2 g of 2-(L-arabotetrahydroxybutyl)-naphth [1, 2] imidazole was added 2 ml of pyridine and 2 ml of acetic anhydride. The mixture was stirred until complete solution was obtained, allowed to stand for an hour, and then poured into water. The obtained crystalline product was filtered and recrystallized from aqueous alcohol. The compound was obtained as glistening colorless crystals with m. p. 178–179°. Yield 0.22 g (70%).

Found %: N 6.02, 6.17. $C_{23}H_{24}O_8N_2$. Calculated %: N 6.14.

Oxidation of 2-(L-arabotetrahydroxybutyl)-naphth [1, 2] imidazole. A suspension of 0.9 g of 2-(L-arabotetrahydroxybutyl)-naphth [1, 2] imidazole in 65 ml of 6% hydrogen peroxide solution was heated to 70–75° and the obtained solution was treated with 2 g of NaOH; the reaction mixture was diluted with an equal volume of water and then heated for 1 hr on the boiling water bath until all of the precipitate had dissolved. Then the solution was boiled with activated carbon, filtered, and the filtrate was treated with hydrochloric acid until weakly acid. Cooling of the solution gave naphth [1, 2] imidazole-2-carboxylic acid as a faintly yellow crystalline product with m. p. 163°. Yield 0.26 g (40%).

*With the assistance of A. I. Butenko.

Found %: N 13.06, 13.14. Acid number 4.2 ml, 4.23 ml 0.1 N NaOH. $C_{12}H_9O_2N_2$. Calculated %: N 13.20, Acid number 4.35 ml 0.1 N NaOH.

Decarboxylation of naphth [1, 2] imidazole-2-carboxylic acid. Naphth [1, 2] imidazole-2-carboxylic acid was heated in an oil bath at 200–210° for 10 min, after which the residue was recrystallized from benzene by the addition of petroleum ether. The product was obtained as yellow crystals with m. p. 176–177°. The mixed melting point with authentic naphth [1, 2] imidazole [7] was not depressed.

2-(D-Galactopentahydroxyamyl)-naphth [1, 2] imidazole hydrochloride. A mixture of 1 g (0.0064 mole) of 1,2-naphthalenediamine and 1.45 g (0.0032 mole) of calcium galactonate hydrate in 25 ml of 2N hydrochloric acid solution was refluxed for 5 hr. The solution was then boiled with activated carbon until colorless, and the filtrate was cooled. The obtained colorless crystals were filtered and then recrystallized from a little water, m. p. 228° (decompn.). Yield 1.1 g (50%).

Found %: N 7.53, 7.61; Cl 9.76, 9.81. $C_{16}H_{19}O_5N_2Cl$. Calculated %: N 7.39; Cl 10.01.

2-(D-Galactopentahydroxyamyl)-naphth [1, 2] imidazole. Treatment of a water solution of 2-(D-galactopentahydroxyamyl)-naphth [1, 2] imidazole hydrochloride with ammonia gave the free base as a colorless powder with m. p. 238–239° (decompn.).

Found %: N 8.71, 8.77. $C_{16}H_{19}O_5N_2$. Calculated %: N 8.96.

Oxidation of the compound with alkaline hydrogen peroxide solution gave naphth [1, 2] imidazole-2-carboxylic acid.

2-(D-Xylotetrahydroxybutyl)-naphth [1, 2] imidazole. Using the above described method A, the condensation of 1.58 g (0.01 mole) of 1,2-naphthalenediamine with 1.95 g (0.005 mole) of calcium D-xylionate hydrate gave 1.17 g of a light-brown product. The compound, purified by boiling with methanol, was obtained as a yellow powder. Weight 0.25 g (3.6%). The product decomposes above 360° without first melting.

Found %: N 9.15, 9.22. $C_{15}H_{16}O_4N_2$. Calculated %: N 9.72.

Analogous results were obtained when the components were condensed employing method B.

SUMMARY

1. The reaction of 1,2-naphthalenediamine with the calcium salts of L-arabonic, D-galactonic and D-xylonic acids gave the corresponding 2-(aldopolyhydroxyalkyl)-naphth [1, 2] imidazoles.

2. Oxidation of the obtained products with alkaline hydrogen peroxide solution leads to the formation of naphth [1, 2] imidazole-2-carboxylic acid.

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REACTION OF DIALKYLAMINOETHANOLS WITH PHOSPHORIC AND THIOPHOSPHORIC ACID ESTERS

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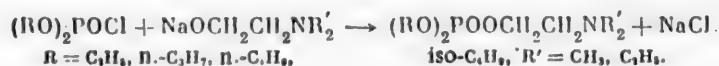
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Organophosphorus compounds, containing amino groupings in the alcohol radical, exhibit high insecticidal activity and systemic action [1-3]. The dialkylaminoethanol derivatives of thiophosphoric acid [4, 5] have received the greatest study.

Phosphoric and thiophosphoric acid derivatives, containing mixed radicals, have not been reported up to now. For this reason it seemed of interest to synthesize and study the properties of some dialkylaminoethyl alkyl phosphates and thiophosphates. The indicated compounds are obtained by the following exemplary equation:



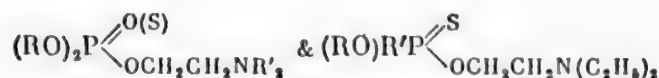
The obtained compounds are oily liquids ranging in color from yellow to brown. Some of them are colorless oils, insoluble in water and ether, and readily soluble in alcohol, benzene, and acetone. The physical constants, analysis data and yields of the synthesized dialkylaminoethyl alkyl phosphates and thiophosphates are given in the table.

EXPERIMENTAL

Into a flask fitted with a reflux condenser, mechanical stirrer and dropping funnel was charged 0.1 mole of either β -dimethyl- or β -diethylaminoethanol, 0.1 mole of metallic sodium and 60-70 ml of dry benzene, and the mixture was heated until all of the sodium had dissolved. Then the reaction mass was cooled to room temperature and treated slowly (in drops), under cooling, with an equimolar amount of the appropriate alkyl or dialkyl phosphate or thiophosphate. The reaction was exothermic and the temperature rose to 40-45°. To complete the reaction, the mixture was heated on the boiling water bath for 2 hr and then was allowed to stand overnight. The next day the sodium chloride was removed either by filtration or by washing with water. The benzene solution was dried over anhydrous sodium sulfate, the solvent distilled off, and the residue was fractionally distilled in vacuo.

SUMMARY

In order to study the insecticidal activity of some phosphoric and thiophosphoric acid esters we synthesized 10 new compounds with the general formula:



Dialkylaminoethyl Alkyl Phosphates and Dialkylaminoethyl Alkyl Thiophosphates



Formula of compound	R	R'	Boiling point (pressure in mm)	d ₄ ²⁰	n _D ²⁰	MR _D		n _D		% l.		Yield (in %)
						found	cal- culated	found	cal- culated	found	cal- culated	
(I)	C ₂ H ₅	C ₂ H ₅	109—110° (2)	1.0612	1.4345	61.89	62.12	249.5	251.98	12.46	12.31	84.5
(I)	C ₂ H ₅	CH ₃	98 (2)	1.0552	1.4160	52.48	52.15	218.2	224.98	13.34, 12.68	13.07	87.5
(I)	n-C ₃ H ₇	C ₂ H ₅	90—91 (4)	0.9639	1.2182	73.96	74.30	282.5	280.9	11.25	11.03	73.2
(I)	n-C ₄ H ₉	C ₂ H ₅	121—122 (4)	0.9770	1.4295	81.95	82.30	300.0	309.0	10.39	10.01	82.3
(I)	n-C ₄ H ₉	CH ₃	106—107 (4)	0.9560	1.4230	74.85	74.40	273.1	281.0	11.02	10.98	82.3
(I)	iso-C ₄ H ₉	C ₂ H ₅	106—107 (3)	0.9594	1.4186	74.05	73.95	281.2	281.0	11.02	11.23	72.4
(I)	iso-C ₄ H ₉	CH ₃	122—123 (5)	0.9725	1.4230	82.50	82.30	315.1	303.0	10.01	10.31	71.3
(II)	CH ₃	C ₂ H ₅ O	70 (4)	1.0907	1.4545	63.72	63.13	263.4	256.0	12.02	12.61	81.60
(II)	n-C ₃ H ₇	(C ₂ H ₅) ₂ N	147—150 (1)	1.008	1.475	84.92	85.30	311	310	10.23	10.00	60.00
(II)	iso-C ₃ H ₇	(C ₂ H ₅) ₂ N	136—137 (4)	0.999	1.473	85.48	85.39	307	310	9.97	10.00	62.00

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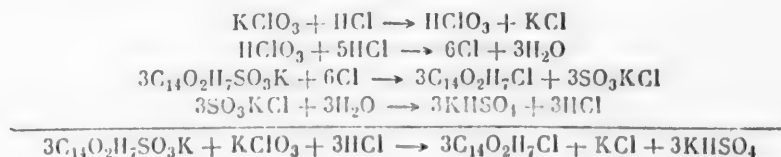
ANTHRAQUINONE SERIES

XXVIII. PECULIARITIES OF THE CHLORINATION OF 1-ANTHRAQUINONESULFONIC ACID WITH CHLORATES*

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The chlorination of anthraquinonesulfonic acids in dilute hydrochloric acid solution with chlorates leads to smooth replacement of the sulfo group by chlorine [1, 2]. Of all of the methods for the preparation of chloroanthraquinones, this method has proved to be the most suitable technically. The reaction is run by the slow addition, at 60-102°, of chlorate solution to a hydrochloric acid solution of the anthraquinonesulfonic acid salt. If possible, the reactions are omitted, then the over-all action of the chlorate on the anthraquinonesulfonic acid in acid medium can be depicted by the scheme:



Despite the great importance of this reaction for the production of chloroanthraquinones, and also in analytical practice, to establish the concentration and nature of the anthraquinonesulfonic acid [3], the reaction of replacing the sulfo group by chlorine employing the technique of oxidative chlorination has failed to be adequately elucidated in the scientific literature. Even such early investigators as M. A. Il'inskii [4] and W. Anderau [2] mentioned the importance of nascent chlorine for this reaction, but the mechanism of the reaction and its general scheme, given above, failed to find a detailed discussion in the literature. The reaction conditions, both on a technical scale and analytically, usually require a consumption of the reagents that is substantially in excess of theory and, in addition, large volumes of the medium and a long reaction time. Recently N. S. Dokunikhin [5], confirming the importance of nascent chlorine, advocated the radical mechanism for the process of replacing the sulfo group in anthraquinonesulfonic acids.

We made a detailed study of the effect of various factors on replacing the sulfo group in 1-anthraquinonesulfonic acid by chlorine. In contrast to the technique usually used in practice of gradually adding the chlorate solution beneath the reaction liquid, we mixed the boiling hot solutions of all of the reagents at the start of the process. We devoted most attention to the importance of the concentration of the reactants and the nature of the medium for the chlorination process. To establish the role of the hydrochloric acid concentration we ran some experiments in which the K-salt of 1-anthraquinonesulfonic acid (1.31 g, 0.004 mole) was reacted with potassium chlorate in 200 ml of HCl, varying the normality of the latter from 0.1 to 3.0N, which means

*For Communication XXVII see Zavodskaya Lab. 25, 926 (1959).

that the amount of acid varied from 0.02 to 0.6 mole. The best yields of the chloroanthraquinone were obtained at an optimum hydrochloric acid concentration of 0.7–0.9N and the use of 40 moles of HCl per mole of the anthraquinonesulfonic acid. The dependence of the chlorination on the concentration and amount of HCl is shown in Fig. 1. An increase in the volume of the solution, with the concentration of both the HCl and the chlorate kept

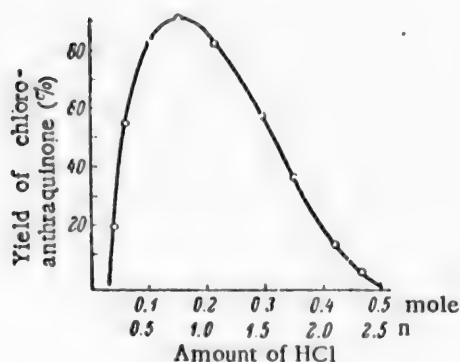


Fig. 1. Chlorination of 1-anthraquinone-sulfonic acid. Effect of hydrochloric acid concentration. 1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 0.89 g KClO_3 (0.0073 mole); 200 ml; 1 hour; 101°.

constant, i. e., increasing their amount based on the weight of taken 1-anthraquinonesulfonic acid salt, favors an increase in the yield of the chloroanthraquinone. From the data in Table 1 it can be seen that at large HCl concentrations, assuring an adequate excess of acid, the difference in the yields of the chloroanthraquinone as a function of change in the volume of the mixture becomes much smaller. Maintaining the amounts of hydrochloric acid and chlorate constant, but varying their concentration in the solution, leads to a change in the yields of the chloroanthraquinone. Thus, the use of 100 ml of 0.7N HCl (0.07 mole) per 1.31 g of potassium 1-anthraquinonesulfonate (0.004 mole) leads to a chloroanthraquinone yield of 78.84%, while the use of the same amounts of HCl and chlorate, but diluting 3.5 times (350 ml), reduces the yield of the chloroanthraquinone to 3.2%. The rate of the process and the yield of the chloroanthraquinone also depend on the concentration of the chlorate and its amount relative to the anthraquinonesulfonic acid and the hydrochloric acid. In the original directions the chlorate was taken in a 9-fold excess of theory, and then later it was reduced to a 3-fold excess [6]. The data on the effect of varying the amount of chlorate are given in Table 2. A considerably higher hydrochloric acid concentration is required when comparatively small amounts of chlorate are taken, and, in reverse, with a substantial excess of the chlorate the reaction goes with a hydrochloric acid of lower concentration. Thus, the same yield (87%) of 1-chloroanthraquinone can be obtained using 0.45N HCl (0.09 mole, 25-fold excess) and 0.004 mole of KClO_3 (3-fold excess), or using 0.25N HCl (0.05 mole, 13-fold excess) and 0.032 mole of KClO_3 (25-fold excess). As a result, the process for replacing the sulfo group by chlorine depends on the optimum concentration of hydrochloric acid and chlorate, assuring the necessary concentration of active chlorine, the rate of its formation, and its reaction with the sulfo group.

Having established the importance of the concentration and amount of hydrochloric acid in replacing the sulfo group by chlorine, we ran a series of experiments in which we studied the effect of adding other acids to the hydrochloric acid reaction medium. Adding different acids in constant amount (57.5 mg-equiv.) exerts a variable effect on the yield of the chloroanthraquinone (Table 3). A further increase in the amount of any of the mineral acids favors an increase in the yield of the chloroanthraquinone. Thus, for example, increasing the amount of phosphoric acid from 0.019 (Table 3) to 0.19 mole increases the yield of 1-chloroanthraquinone from 26.9 to 45.5%.

The use of hydrochloric acid-sulfuric acid mixtures was studied in greater detail by us. From the results of these experiments, listed in Table 4, it can be seen that increasing the amount and concentration of the sulfuric acid leads to a substantial increase in the rate of the process. If the chloroanthraquinone is not formed when the hydrochloric acid concentration is 0.5N, then the addition of sulfuric acid (0.105 mole) to give a mixed acid concentration of 1.1N already gives a 19.2% yield of the chloroanthraquinone. The beneficial effect of the sulfuric acid in such mixtures has its limit, the same as in the case of pure hydrochloric acid. When the sulfuric acid concentration exceeds 3N both the rate of the process and the yield of the chloroanthraquinone begin to drop. The over-all equation for the chlorination reaction in the presence of sulfuric acid can be depicted by the scheme:



An analytical study of the reaction solution before and after chlorination of the K-salt of 1-anthraquinone-sulfonic acid, both in the experiments using hydrochloric acid alone and using hydrochloric acid-sulfuric acid mixtures, revealed that the total acidity of the medium remained practically constant; the total consumption of liberated chlorine at low hydrochloric acid concentrations (up to 0.2N) is in agreement with the above given

TABLE 1

Chlorination of 1-Anthraquinonesulfonic Acid With Chlorate. Effect of the Volume of Hydrochloric Acid at Constant Concentration [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 0.15N and 0.35N HCl; KClO_3 7.5 g/liter; 2 hr; 101°]

HCl (in ml)	Amount*		Yield of chloroanthra- quinone (in %)
	HCl	KClO ₃	
0.15N HCl			
100	4-fold	5-fold	5.81
200	8-fold	10-fold	16.78
600	24-fold	30-fold	38.39
0.35N HCl			
100	12-fold	5-fold	76.87
200	24-fold	10-fold	82.96
600	72-fold	30-fold	93.0

TABLE 2

Chlorination of 1-Anthraquinonesulfonic Acid. Effect of the Amount of Chlorate [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 200 ml of HCl; 2 hr; 101°]

KClO ₃		HCl		Yield of chloro- anthraquinone (in %)
(g)	(mole)	(mole)	normality	
For different HCl concentrations				
0.5	0.004	0.03	0.15	6.1
0.5	0.004	0.05	0.25	46.41
0.5	0.004	0.09	0.45	85.84
1.5	0.012	0.03	0.15	22.75
1.5	0.012	0.05	0.25	64.48
1.5	0.012	0.06	0.30	73.82
1.5	0.012	0.07	0.35	81.32
1.5	0.012	0.09	0.45	93.05
For constant HCl concentrations				
0.5	0.004	0.06	0.3	51.41
1.0	0.008	0.06	0.3	64.40
1.5	0.012	0.06	0.3	73.82
2.0	0.016	0.06	0.3	81.60
0.5	0.004	0.09	0.45	85.84
1.0	0.008	0.09	0.45	93.05
1.5	0.012	0.09	0.45	94.50
2.0	0.016	0.09	0.45	96.88

reaction schemes. On the average, the consumption of chlorine from the chlorate is 54% of the consumption of chlorine from the hydrochloric acid. At higher hydrochloric acid concentrations the total chlorine consumption increases by 10–20%.

The addition of organic acids, and, in particular, of acetic acid, operates in different manner. If, at constant amounts (in mg-equiv.), the use of acetic acid gives the chloroanthraquinone in a yield that is 1/2 that obtained using phosphoric acid, and 1/6 that obtained using hydrochloric acid, then a further increase in the amount of acetic acid causes the yield of the reaction product to decrease even more (in %): at 0.057 mole—13.3, 0.095 mole—11.6, and 0.21 mole—9.3; at 0.55 mole the chloroanthraquinone is no longer formed. The acetic acid homologs—propionic and n-butyric acid—stop the chlorination when used in even smaller amounts. As a result, despite the presence of hydrochloric acid (0.04 mole) in the reaction medium, by itself securing a 20.17% yield of the chloroanthraquinone, the addition to it of various amounts of carboxylic acids gradually stops the process of replacement of the sulfo group by chlorine. It should be mentioned

that in many of the experiments where organic acids were used, despite the absence of a chloroanthraquinone yield, a noticeable evolution of chlorine was always observed. What is the function of acids in a hydrochloric acid mixture? It is known that the sulfo group in 1-anthraquinonesulfonic acid can be replaced by chlorine by

*Relative to the amount required by theory.

TABLE 3

Effect of Nature of Acid on Chlorination of K-salt of 1-Anthraquinonesulfonic Acid [1.31 g of K-salt (0.004 mole); 0.894 g KClO_3 (0.0073 mole); 0.04 mole HCl (0.2N); 57.5 mg-equiv. of added acid; normality of acid mixture 0.49N; 200 ml; 1 hr; 101°]

Acid		Yield of chloro-anthraquinone (in %)
name	(mole)	
—	—	20.17
HCl	0.057	82.15
HNO_3	0.057	70.6
H_2SO_4	0.029	55.62
H_3PO_4	0.019	26.98
H_3BO_3	0.019	23.9
CH_3COOH	0.057	13.26
CCl_3COOH	0.057	6.98
$\text{C}_6\text{H}_7\text{COOH}(\text{n.})$	0.057	1.23

TABLE 4

Effect of Adding Sulfuric Acid on the Chlorination of the K-salt of 1-Anthraquinonesulfonic Acid [1.31 g of K-salt (0.004 mole); 0.894 g KClO_3 (0.0073 mole); 200 ml; 1 hr; 102°]

H_2SO_4 (in mole)	Total normality of acids in solution	Yield of chloro-anthraquinone (in %)
For 0.01 mole of hydrochloric acid (0.05 N)*		
0.105	1.10	19.20
0.125	1.29	28.92
0.201	2.06	77.18
0.230	2.35	84.23
0.277	2.82	92.81
For 0.04 mole of hydrochloric acid (0.2 N)**		
0.0095	0.29	35.21
0.029	0.49	55.62
0.048	0.68	68.67
0.105	1.25	86.86
0.124	1.44	89.41
0.201	2.21	97.18
0.277	2.97	98.22

chloric acid alone or in admixture with other mineral acids is used, also depends on the hydrogen-ion concentration in the medium (Table 5). The yields of the chloroanthraquinone were practically the same in the experiments where the hydrogen-ion concentration was maintained constant while varying the concentration of the mixtures of hydrochloric acid with other mineral acids. A substantial increase in the concentration of the acids when compared with the optimum changes the character of the chlorinating agent, lowers its solubility and reduces the polarization of the sulfo group. Usually a copious evolution of molecular chlorine is observed at high mineral acid concentrations.

*The chloroanthraquinone is not formed when only the HCl solution is used.

**The chloroanthraquinone was obtained in 20.17% yield when only the HCl solution was used.

direct reaction with gaseous chlorine, which is passed into a hydrochloric acid solution of 1-anthraquinonesulfonic acid [1, 7]. However, here the chlorination goes slowly, and the yield of the chloroanthraquinone is low. Only by creating a certain concentration of active chlorine in the solution is it possible to effect a complete replacement of the sulfo group by chlorine. It is known that the sulfo group is easily replaced by the active chlorine that is liberated when a hydrochloric acid solution of the anthraquinonesulfonic acid is exposed to the action of light [8]. A sharp increase in the formation rate of the chloroanthraquinone when using gaseous chlorine in hydrochloric acid medium is observed if the reaction solution is exposed to the illumination from a mercury-vapor lamp, and finally, the formation rate is increased under the influence of initiating substances, which decompose under the reaction conditions with the formation of free radicals [5]. It should be mentioned that the action of these initiators when chlorination is with chlorate in hydrochloric acid solution is manifested to less degree than when reaction is with gaseous chlorine [5]. The chlorate in itself assures obtaining the necessary amount of active chlorinating agent. In the oxidative chlorination of anthraquinonesulfonic acids the acidity of the medium favors the formation of active chlorine, polarization of the sulfo groups (at the C-S linkage), and reaction of the formed radicals. The peculiar reactivity of the sulfo groups in anthraquinonesulfonic acids, differentiating them from many aromatic sulfonic acids, is determined in oxidative chlorination, as well as in a number of other reactions (replacement by OH , NO_2 , etc.), by the highly electrophilic nature of the carbon atom attached to the sulfo group (especially in the 1-position).

The fastest rate for the reaction of replacing the sulfo group by chlorine, observed when the optimum concentration of hydro-

TABLE 5

Effect of Hydrogen Ion Concentration on the Chlorination of the K-salt of 1-Anthraquinonesulfonic Acid [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 0.06 mole of HCl; 0.9 g of KClO_3 (0.0074 mole); 200 ml; 1 hr; 101°]

H_2SO_4 (in mole)	Total normality of acids in solution		H^+ -ion concentration (g-ion/liter)	Yield of chloroanthra- quinone (in %)
	Before reaction	After reaction		
—	0.302	0.300	0.269	46.14
0.019	0.398	0.400	0.319	46.9
0.057	0.588	0.588	0.408	55.78
0.095	0.778	0.780	0.498	59.78
0.171	1.158	1.150	0.727	73.84

TABLE 6

Effect of Chlorides and Sulfates on the Chlorination of 1-Anthraquinonesulfonic Acid With Chlorate in HCl medium [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 0.894 g of KClO_3 (0.0073 mole); 200 ml; 1 hr; 101°]

Salt		Yield of chloro-anthraquinone (in %)
formula	amount (mole)	
For 0.04 mole of HCl (0.2 N)		
—	—	21.68
MgCl ₂	0.028	32.47
ZnCl ₂	0.032	None
Na ₂ SO ₄	0.048	Likewise
MgSO ₄	0.04	"
ZnSO ₄	0.025	"
For 0.06 mole of HCl (0.3 N)		
—	—	56.88
KCl	0.02	59.0
NH ₄ Cl	0.02	56.61
CaCl ₂	0.01	58.19
MgCl ₂	0.01	52.2
AlCl ₃	0.008	57.80
CuCl ₂	0.01	29.38
FeCl ₃	0.007	8.76
Na ₂ SO ₄	0.01	43.16
Na ₂ SO ₄	0.03	None
MgSO ₄	0.01	30.55
K ₂ SO ₄	0.01	43.80
ZnSO ₄	0.025	None
Fe ₂ (SO ₄) ₃	0.003	4.89

All that has been said above can be compared very successfully with the dielectric constant and the degree of dissociation of acids. The higher these constants are for mineral acids, the more successful is the replacement of the sulfo group by chlorine. The introduction into the hydrochloric acid medium of organic acids with a variable degree of dissociation, but nearly with the same low dielectric constant, sharply reduces the effect of replacing the sulfo group by chlorine.

As is known, the introduction of halogen into the anthraquinone nucleus and many of its derivatives is frequently effected by using chlorine in concentrated or fuming sulfuric acid, glacial acetic acid, alcohol, carbon disulfide, or nitrobenzene [9]. A redistribution of the electron density in the compound occurs under these conditions, the sulfo group is no longer capable of being replaced by the chlorine atom, and for this reason the possibility of introducing chlorine into the anthraquinone nucleus becomes favorable, especially if substituents are present, including the sulfo group [10]. This replacement of hydrogen in the anthraquinone is made considerably easier if such a substituent as the hydroxy group is present [4].

The presence of a number of metal salts also exerts an effect on the process of replacing the sulfo group in anthraquinonesulfonic acids by chlorine, irrespective of whether the chlorination is with gaseous chlorine using initiators [5], or using chlorate. The chlorides and sulfates of iron, copper, zinc and manganese exert a marked inhibiting effect. The chlorides of such metals as Na, K, Ca, Mg and Al, taken in amounts up to 5 to 10 moles per mole of anthraquinone-

sulfonic acid, either exert no effect, or favor an increase in the yield of 1-chloroanthraquinone (Table 6). The sulfates of these metals begin to show an inhibiting effect when taken in amounts of 1.5 to 2.0 moles per mole of anthraquinonesulfonic acid. The addition of sodium chloride to the hydrochloric acid reaction medium noticeably accelerates the chlorination process and increases the yield of the chloroanthraquinone. This circumstance makes it possible to reduce the consumption of hydrochloric acid and to use in practice a mixture of

TABLE 7

Effect of Adding NaCl in the Chlorination of 1-Anthraquinonesulfonic Acid With Chlorate in Hydrochloric Acid Medium [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 0.894 g of KClO_3 (0.0073 mole); 200 ml; 1 hr; 101°]

Amount of NaCl (in mole)	Yield of chloroanthraquinone (in %)
For 0.1 N HCl (0.02 mole)	
—	Traces
0.02	2.16
0.06	7.53
For 0.2 N HCl (0.04 mole)	
—	21.68
0.014	31.55
0.02	36.67
0.029	43.06
0.058	45.56
0.115	48.91
For 0.3 N HCl (0.06 mole)	
—	56.88
0.02	60.82
0.06	57.38

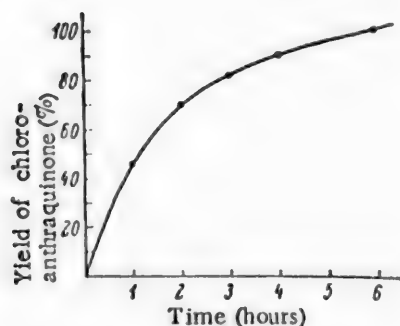


Fig. 2. Chlorination of 1-anthraquinonesulfonic acid. Effect of time. [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 2.5 g of KClO_3 (0.0204 mole); 450 ml of 0.2N HCl; 101°].

nation of 1-anthraquinonesulfonic acid to 1 to 2 hr.

In practice the chlorination is usually run at the boiling point of the hydrochloric acid solution, which corresponds to 100–102°. Reducing the temperature to 95° causes the yield of 1-chloroanthraquinone to drop by a matter of 2.5–3 times. At high hydrochloric acid concentrations, securing, as was indicated above, a substantial reaction rate, reducing the reaction temperature leads to a smaller reduction in the yield of 1-chloroanthraquinone (down to 30%). Reducing the chlorination temperature exerts an even smaller effect on the

acid and common salt with a lower corrosive action than that shown by hydrochloric acid alone (Table 7). Hardly any influence is exerted by sodium chloride at high hydrochloric acid concentrations (above 0.3N).

As is known, for the oxidative chlorination of anthraquinone-sulfonic acids it is recommended to use a mixture of sulfuric acid and common salt [4]. In many cases it was recommended to use such a system for the purpose of accelerating the chlorination because of the ability to substantially raise the temperature of the reaction medium up to 110–140° [4]. However, M. A. Il'inskii has observed that the action of the sulfuric acid is not limited specifically to being able to raise the temperature [4].

The experiments on the chlorination of 1.31 g (0.004 mole) of the K-salt of 1-anthraquinonesulfonic acid for 1 hour in 200 ml of 4.6N sulfuric acid (0.46 mole) solution, containing from 0.01 to 0.06 mole of sodium chloride, gave a quantitative yield of the chloroanthraquinone. The sulfates and bisulfates that are formed here do not exert an inhibiting effect on the chlorination process, in contrast to what has been said above for hydrochloric acid alone. It is expedient to use a mixture of hydrochloric and sulfuric acids when operating with anthraquinonesulfonic acid salts contaminated with sulfates and, in particular, in the analytical characterization of the former by the technique of their complete conversion to chloroanthraquinones.

Despite the fact that in the generally accepted method of chlorinating anthraquinonesulfonic acids the hydrochloric acid mother liquor remaining after separation of the chloroanthraquinone contains substantial amounts of hydrochloric acid and chlorate, the reuse of these materials is attended by difficulties. Increasing the concentration of mineral salts in the solution retards the new chlorination operation and lowers both the yield and the quality of the chloroanthraquinone. The use of mixtures of hydrochloric acid or common salt with sulfuric acid for the chlorination makes it possible to reuse the mother liquors. By adding either hydrochloric acid or common salt and chlorate to these mother liquors until the original concentrations are reached, it becomes possible to make repeated chlorinations without reducing either the yield or the quality of the formed chloroanthraquinone.

The important factors in the process for the chlorination of 1-anthraquinonesulfonic acid are the time and the temperature. Despite the fact that the rate of the process depends on the hydrochloric acid concentration (or that of the sulfuric acid in acid mixtures), the dependence of the chloroanthraquinone yield on the time has approximately the same character in all cases and is shown in Fig. 2. By choosing the optimum conditions and, in particular, the hydrochloric acid concentration, or that of its mixture with either sulfuric or phosphoric acid, it becomes possible to sharply increase the reaction rate and confine the time required for the complete chlori-

TABLE 8

Effect of Temperature in the Chlorination of the K-salt of 1-Anthraquinonesulfonic Acid [1.31 g of K-salt of 1-anthraquinonesulfonic acid (0.004 mole); 0.894 g of KClO_3 (0.0073 mole); 200 ml; 1 hr]

Temperature	Normality of solution		Yield of chloroanthraquinone (in %)
	HCl	H_2SO_4	
95°	0.3	—	23.8
102	0.3	—	59.41
95	0.8	—	66.86
102	0.8	—	93.89
78	0.08	5.76	5.25
97	0.08	5.76	96.27
100	0.08	5.76	96.34
107	0.08	5.76	94.64
78	0.69	2.6	4.56
97	0.69	2.6	89.60

yield of the chloroanthraquinone if hydrochloric acid-sulfuric acid mixtures are used. Here the chlorination already begins at 75–80°, whereas 1-chloroanthraquinone is not formed under these conditions in pure hydrochloric acid medium (Table 8).

SUMMARY

1. The process of replacing the sulfo group in anthraquinonesulfonic acids by chlorine by the technique of oxidative chlorination depends on many factors and, in particular, on the concentration of the hydrochloric acid or of the mixed acids. The intensity of the action exerted by the acids added to the hydrochloric acid solution depends on their degree of dissociation and, in particular, on the dielectric constant. An optimum acidity of the medium facilitates increasing the active chlorine concentration, leads to substantial polarization of the sulfo group and a faster rate of forming the chloroanthraquinone.

2. Organic carboxylic acids inhibit the oxidative chlorination of anthraquinonesulfonic acids.

3. A study was made of the effect of mineral acids on the reaction of replacing the sulfo group in 1-anthraquinonesulfonic acid by chlorine.

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REACTION OF THIOUREA WITH N-(α -BROMOACYL) AMINO ACIDS

I. REACTION OF THIOUREA WITH N-(α -BROMOBUTYRYL) GLYCINE IN ETHYL ALCOHOL

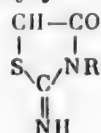
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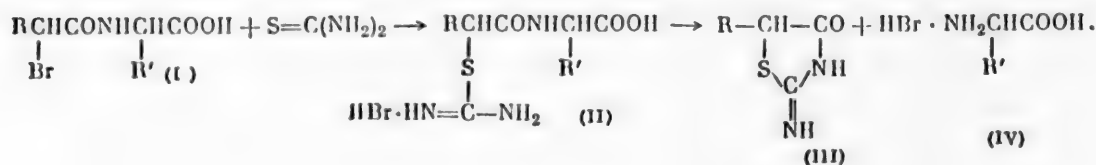
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10, pp. 3464-3468, October, 1960

Original article submitted October 5, 1959

Interest in thiourea derivatives is justified by the high biological activity shown by many of them [1]. We studied the reaction of thiourea with N-(α -bromoacyl) amino acids from the standpoint of being able to obtain the corresponding N-(α -isothiuroniumacyl) amino acids. Such compounds are not described in the literature. Of the papers devoted to analogous reactions, of interest are those where the reaction of thiourea with the amides of monochloroacetic acid is discussed. It was found [2] that the reaction of mono- and diphenylthiourea with amides of type $\text{ClCH}_2\text{CONHR}$, where $\text{R} = \text{C}_6\text{H}_5$ or $\text{o-NO}_2\text{C}_6\text{H}_4$, in boiling ethanol gives the corresponding N-substituted pseudothiohydantoins, for example



where $\text{R} = \text{C}_6\text{H}_5$. It was shown [3] that if NHR was either the 2-aminopyridine or the 2-aminothiazole moiety, then in this case the reaction goes with the formation of the corresponding isothiuronium compounds. The reaction of thiourea with N, N-dipropyl-2-chloroacetamide in boiling alcohol gives pseudothiohydantoin (86% yield) and dipropylamine (74% yield) [4]. Since in our work the starting bromoacylamino acids are to a certain degree analogous to substituted amides, then it was possible to postulate the following scheme for the reaction:



We selected N-(α -bromobutryl) glycine as the main subject of study. When the reaction of this compound with thiourea in boiling ethanol was studied it was found that after 7 hr the yield of 5-ethylpseudothiohydantoin (III) is 72%, while the amount of cleaved glycine is 69%. We used S-labeled thiourea in the reaction, and the method of paper radiochromatography was used to analyze the reaction mixture. It proved that the graph of the activity distribution (Fig. 1) exhibits a maximum, corresponding to the substance with R_f 0.27, not belonging to any of the identified components of the reaction, and apparently corresponding to N-(α -isothiuroniumbutyryl) glycine (II). However, the amount of this substance in the reaction mixture does not exceed 7.5%. The introduction of substituents in the amino acid or in the acyl moiety fails to alter the course of the reaction. Thus,

Products of the Reaction of Some N-(α -Bromoacyl) amino Acids RCHCONHCH(R')COOH

with Thiourea in Alcohol Solution

R	R'	Reaction time (in hours)	Reaction temperature	Compounds formed					
				pseudothiohydantoin (III)		II ^a		amino acid hydrobromide (IV)	
				Yield (%)	R _f	Yield (%)	R _f	Yield (%)	R _f
C ₂ H ₅	H	168	17°	11 ^b	0.74	9 ^b	0.27	+ ^c	0.05
C ₂ H ₅	H	7	78	32 ^b	0.74	7.5 ^b	0.27	+	0.05
C ₂ H ₅	H	7	78	72	0.74	+	0.27	69	0.05
CH ₃	H	7	78	+	0.85	—	—	54	0.05
CH ₃	CH ₃	7	78	62	0.85	+	0.18	58	0.10
(CH ₃) ₂ CH	H	7	78	+	0.54 ^d	—	—	+	0.20 ^d
C ₄ H ₉	H	7	78	+	0.87 ^d	—	—	+	0.20 ^d

a) Postulated reaction product. b) The data were obtained by the method of radiochromatography without isolating the substances from the reaction mixture. c) A + sign means that the substance is present in the reaction mixture, while a - sign means that the substance could not be detected chromatographically. d) In this case the R_f values are given for a mixture of butanol—acetic acid—water, and in all of the other cases—for water-saturated butanol.

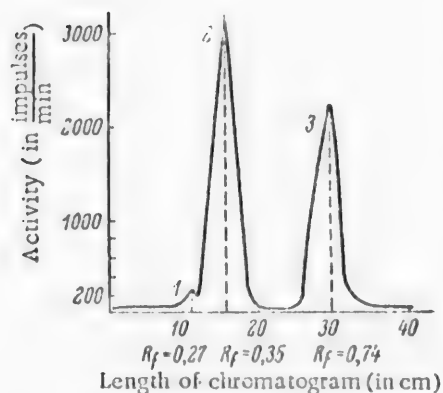


Fig. 1. Distribution of the activity on chromatogram (ascending method, solvent—water-saturated butanol) 3 hr after the start of reaction of thiourea-S³⁵ with N-(α -bromobutyl) glycine in boiling ethanol. 1) N-(α -isothiuroniumbutyl) glycine (postulated reaction product); 2) thiourea; 3) 5-ethylpseudohydantoin.

when thiourea is reacted with N-(α -bromopropionyl) alanine for 7 hr in boiling ethanol the yield of 5-methylpseudothiohydantoin is 62% and that of alanine is 58%. By chromatography it was shown that glycine is cleaved and the corresponding pseudothiohydantoin is formed when thiourea is reacted with N-(α -bromopropionyl)-, N-(α -bromo-isovaleryl), and N-(α -bromohexanoyl)-glycine. Only the reaction rate changes if the reaction is run at room temperature, while the yield of the postulated N-(α -isothiuroniumbutyl) glycine fails to increase.

EXPERIMENTAL

The starting N-(α -bromoacyl) amino acids were obtained by the E. Fischer method [5], by reacting the acid bromides of the corresponding α -bromocarboxylic acids with amino acids. The substituted pseudothiohydantoins, used as "witnesses" during chromatographing were obtained by the method [6] described in the literature, from thiourea and α -bromocarboxylic acids.

Reaction of thiourea with N-(α -bromobutyl) glycine in alcohol. A solution of 3.8 g of thiourea and 11.2 g of N-(α -bromobutyl) glycine in 100 ml of boiling ethanol was heated under reflux for 7 hr. The method of paper chromatography [paper—Whatman No. 1, Type "B"; solvent—water-saturated butanol or the organic layer of a mixture of butanol, acetic acid and water (4:1:5); color reagents: ninhydrin solution, solution of benzidine and potassium iodide, Grote re-

agent] was used to follow the course of the reaction. Samples of the reaction mixture were removed at hour intervals. Analysis revealed that immediately after mixing the starting substances the reaction mixture contains 5-ethylpseudothiohydantoin with R_f 0.85 and glycine (R_f 0.20), whereas for thiourea R_f = 0.50, and for (1) R_f = 0.75 (butanol—acetic acid—water). For water-saturated butanol the R_f are respectively equal to 0.74, 0.05, 0.35, and 0.80, and, in addition, there is a stain with R_f 0.27. On conclusion of reaction the solution was evaporated *in vacuo*.

The obtained glycine hydrobromide was filtered, and the filtrate was treated with hot ethyl acetate to extract the pseudothiohydantoin, which separated on subsequent cooling of the solution. Yield 5.2 g (72%). The substance was identified as the picrate.

Found %: C 35.70, 35.63; H 3.26, 3.16; N 18.22, 18.16. $C_{11}H_{11}O_3N_5S$. Calculated %: C 35.65; H 2.91; N 18.76.

The yield of glycine after alkalization of the hydrobromide was 2.6 g (69%), m.p. 225–227° (decompn.), which agrees with the literature data. For a quantitative estimate of the change in the amounts of the reaction components with time we used the method of paper radiochromatography.

Radiochromatographic study of the reaction of N-(α -bromobutyl)-glycine with thiourea in alcohol solution. A mixture of 0.1480 g of thiourea, containing S^{35} , with a specific activity of 1.27×10^8 impulses/min per 1 g, and 0.44 g of N-(α -bromobutyl) glycine in 45 ml of ethanol was heated under reflux for 4 hr. Samples (0.05 ml) were removed at hourly intervals, and were deposited on paper strips 3 cm wide and then chromatographed in water-saturated butanol for a day. The dried chromatograms were cut into lateral strips 5 mm wide and the activity of each strip was measured under standard conditions using a block counter. The statistical error of the count did not exceed 5%. The results of the measurements are plotted graphically in the coordinates: activity vs. distance from the point of deposition. The curve of the activity showed maxima in the zones corresponding to the sulfur-containing components of the reaction mixture on the chromatograms (Fig. 1). The activities corresponding to each substance were totaled. The amount of each reaction component in the solution at any given moment was determined and expressed in percent. Since the reaction mixture was homogeneous, such determination was equivalent to determining the yields of the substances in mole percent. The data on the amounts of reaction components at any given moment are plotted in Fig. 2. The amount of pseudothiohydantoin steadily increased with time when the reaction was run at room temperature for 7 days. The amount of substance with R_f 0.27 did not exceed 9% and hardly changed with time (Fig. 3).

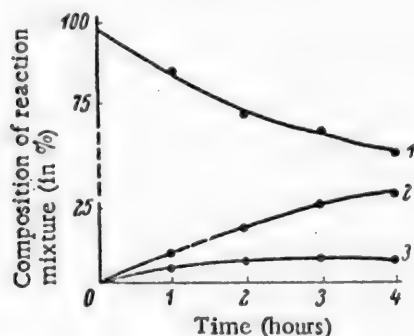


Fig. 2. Change in composition of reaction mixture during reaction of N-(α -bromobutyl) glycine with thiourea in boiling ethanol medium. 1) Thiourea; 2) 5-ethylpseudothiohydantoin; 3) N-(α -isothiuroniumbutyl) glycine (postulated reaction product).

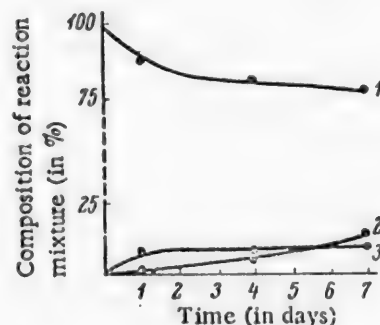


Fig. 3. Change in composition of reaction mixture during reaction of N-(α -bromobutyl) glycine with thiourea in ethanol medium at room temperature. 1) Thiourea; 2) 5-ethylpseudothiohydantoin; 3) N-(α -isothiuroniumbutyl) glycine.

Reaction of thiourea with N-(α -bromopropionyl) alanine in boiling ethanol. A mixture of 2.3 g of thiourea and 7 g of N-(α -bromopropionyl) alanine was dissolved in 100 ml of ethanol and the solution was heated under reflux. After 7 hr the heating was stopped and the alcohol was distilled in vacuo. The residue was dissolved in the minimum amount of water and then the solution was neutralized with 25% NaOH solution, where a white crystalline precipitate of 5-methylpseudothiohydantoin was obtained. Yield 2.5 g (62%), m.p. 204–206° (from water). The mixed melting point with the 5-methylpseudothiohydantoin obtained from α -bromopropionic acid and thiourea was not depressed. After removal of the thiohydantoin precipitate, the filtrate was evaporated to isolate the alanine. Yield 1.6 g (58%), m.p. 288–289° (decompn.), which agrees with the literature data.

Reaction of thiourea with other N-(α -bromoacyl) amino acids. The chromatographic technique was used to make a quantitative study of reacting equivalent amounts of thiourea with N-(α -bromopropionyl)-, N-(α -bromo-isovaleryl)-, and N-(α -bromohexanoyl)-glycine in boiling ethanol. To identify the reaction products during chromatographing we used glycine and the corresponding substituted pseudothiohydantoins as "witnesses". The results of the experiments are given in the table.

SUMMARY

1. It was shown that the reaction of thiourea with N-(α -bromoacyl) amino acids in ethanol goes with the cleavage of amino acid and the formation of the corresponding 5-alkylpseudothiohydantoins (2-imino-4-oxo-5-alkylthiazolidines).
2. For the reaction of thiourea with N-(α -bromobutyl) glycine we used the method of paper radiochromatography to obtain quantitative data on the amounts of components in the reaction mixture at different periods of time. It was shown that the formation of 5-ethylpseudothionydantoin proceeds at a rapid rate. The amount of substance with R_f 0.27, which could be N-(α -isothiuroniumbutyl) glycine, does not exceed 7.5%, and fails to increase noticeably when the reaction temperature is lowered.

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S-DERIVATIVES OF THIOUREA

II. SYNTHESIS OF 2-IMINO-3-ALKYL-5-ISOTHIURONIUMMETHYLTHIAZOLIDINES

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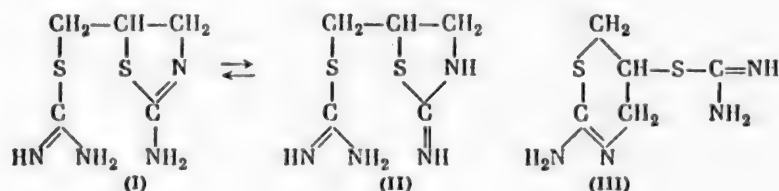
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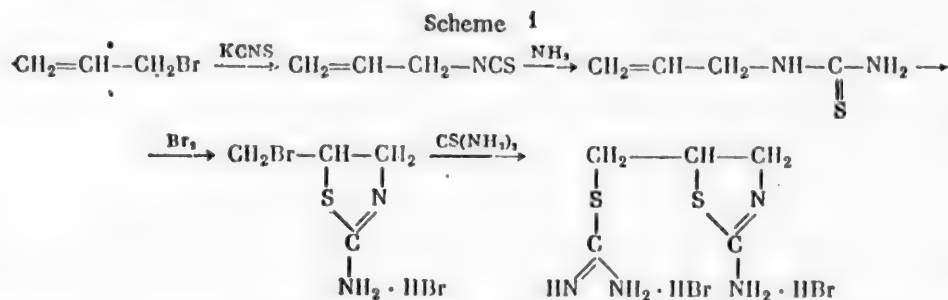
October, 1960

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In the previous communication [1] it was shown that the compound formed in the reaction of thiourea with 2,3-dibromopropylamine is not the expected 2,3-diisothiuroniumpropylamine. Starting with the analysis data, and by analogy with the chemical behavior of 2-iminoethylisothiuronium [2], it was postulated that the compound formed here is 2-amino-5-isothiuroniummethyl- Δ^2 -thiazoline (I), tautomeric with 2-imino-5-isothiuroniummethylthiazolidine (II). However, the possibility of forming 2-amino-5-isothiuroniumpenthiazoline (III) under these conditions was not excluded, by analogy with the cyclization of 3-aminopropylisothiuronium to the corresponding penthiazoline [2].



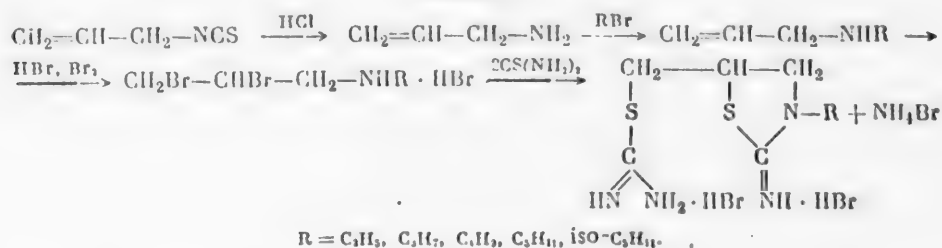
To determine which of the rings is formed in the given case, we prepared the most probable product of the reaction, namely 2-amino-5-isothiuroniummethylthiazoline dihydrobromide, by counter synthesis, in accordance with Scheme 1.



The obtained substance is completely identical with the product obtained from the reaction of thiourea with 2,3-dibromopropylamine hydrobromide, which is confirmed by chromatographic analysis and the absence of mixed melting point depression. As a result, the 5-membered thiazoline ring is formed when thiourea is reacted with 2,3-dibromopropylamine, apparently through the intermediate diisothiuronium derivative.

We were interested in determining what effect replacing one of the hydrogens in the amino group of 2,3-dibromopropylamine by a primary alkyl radical would have on the cyclization. From an analysis of the products obtained when thiourea was reacted with N-monoalkyl-2,3-dibromopropylamines it was established that these products also correspond to the formulas of the corresponding thiazolidines, i.e., replacement of one hydrogen in the amino group by a primary alkyl radical does not prevent cyclization. Employing Scheme 2, we synthesized a number of 2-imino-3-alkyl-5-isothiuroniummethylthiazolidines as the dihydrobromides (by analogy with 2-amino-5-isothiuroniummethylthiazoline, it is assumed that a five-membered ring is also formed in this case).

Scheme 2



The degree of purity of all of the final products was checked by paper chromatography (ascending method). As moving solvent we used the organic layer of the butanol-water-acetic acid mixture, taken in the ratio 4:5:1, while Guinier reagent [3] was used as the color developer, giving with the described compounds a reddish-purple stain, appearing when the chromatograms were heated to 100–120°.

TABLE 1

Properties of N-Alkylallyl amines $\text{CH}_2=\text{CH}-\text{CH}_2-\text{NHR}$

R	Yield (in %)	Boiling point	d_{20}^{20}	n_D^{20}	MR _D		Literature constants			
					found	calculated	boiling point	d_{20}^{20}	n_D^{20}	reference
C ₂ H ₅	46	85–86°	0.7501	1.4153	28.40	28.43	84°	0.7536	1.4145	[7, 10]
C ₃ H ₇	43	107–108	0.7589	1.4242	33.00	33.09	110–114	0.7708	—	[11]
C ₄ H ₉	45	131–132	0.7761	1.4278	37.11	37.71	131	0.7851	1.4297	[7, 12, 13]
C ₅ H ₁₁	46	156–157	0.7773	1.4347	42.30	42.38	156	—	—	[11]
iso-C ₅ H ₁₁	43	148–150	0.7714	1.4301	42.23	42.32	148–153	0.7777	—	[11]

TABLE 2

Hydrobromides of N-Alkyl-2,3-dibromopropylamines
 $\text{CH}_2\text{Br}-\text{CHBr}-\text{CH}_2-\text{NHR}$

R	Yield (in %)	Melting point	
		found	from the literature [8]
C ₂ H ₅	91	138°	135°
C ₃ H ₇	87	190	189–191
C ₄ H ₉	94	230	225
C ₅ H ₁₁	86	253	—
iso-C ₅ H ₁₁	57	230	230–231

TABLE 3

Dihydrobromides of 2-imino-3-alkyl-5-isothiuroniummethylthiazolidines

R	Yield (in %)	Melting point	R_f	Found (%)				Empirical formula
				C	H	N	Br	
C_2H_5	35	186–189°	0.22	22.11, 21.91	4.19, 4.08	14.82, 14.75	42.11, 41.92	$C_7H_{16}N_4S_2Br_2$
C_3H_7	41	218–220	0.25	24.23, 24.17	4.37, 4.59	14.40, 14.35	41.29, 40.59	$C_8H_{18}N_4S_2Br_2$
C_4H_9	29	230	0.36	26.50, 26.61	4.82, 4.86	13.50, 13.31	39.32, 39.02	$C_9H_{20}N_4S_2Br_2$
C_5H_{11}	35	253	0.55	28.31, 28.40	5.05, 4.93	13.52, 13.28	37.79, 37.83	$C_{10}H_{22}N_4S_2Br_2$
iso- C_5H_{11}	40	240	0.50	28.40, 28.45	5.06, 4.98	13.03, 12.99	37.95, 37.90	$C_{10}H_{22}N_4S_2Br_2$

EXPERIMENTAL

Synthesis of 2-Amino-5-isothiuroniummethylthiazoline dihydrobromide. Allyl isothiocyanate was obtained by the reaction of allyl bromide with potassium thiocyanate and subsequent isomerization [4]. B. p. 58–60° (20 mm Hg); yield 80%. N-Allylthiourea was obtained by the reaction of allyl isothiocyanate with aqueous ammonia in alcohol medium [5]. M. p. 74° (from water); yield 75%. 2-Amino-5-bromomethylthiazoline hydrobromide was obtained by the bromination of N-allylthiourea in alcohol medium [6]. M. p. 137° (from water); yield 93%; R_f 0.70.

A solution of 2.76 g of thiourea and 10 g of 2-amino-5-bromomethylthiazoline hydrobromide in 50 ml of anhydrous isobutyl alcohol was refluxed for 1 hour. The obtained precipitate was filtered, dried, and recrystallized from a mixture of methanol and ethanol (1:1). We obtained 8.1 g (65%) of white crystalline compound. M. p. 220°; R_f 0.22.

Found %: C 17.04, 17.20; H 3.39, 3.45; N 15.40, 15.67; Br 45.37, 45.46. $C_5H_{12}N_4S_2Br_2$. Calculated %: C 17.05; H 3.41; N 15.91; Br 45.41.

Synthesis of the dihydrobromides of some 2-imino-3-alkyl-5-isothiuroniummethylthiazolidines. Allylamine was obtained in 80–85% yield by the hydrolysis of allyl isothiocyanate [7]. The alkylallylamines were obtained by reacting allylamine with the appropriate alkyl bromides, followed by fractionation of the obtained mixture of alkyl- and dialkylallylamines [8–13]. The properties of the obtained alkylallylamines, already reported in the literature, are given in Table 1. The hydrobromides of the N-alkyl-2,3-dibromopropylamines were obtained by the bromination of the corresponding alkylallylamine hydrobromides in weakly acid medium [8], followed by recrystallization from isopropyl alcohol. The properties of the obtained dibromides are given in Table 2.

A mixture of 0.05 mole of N-alkyl-2,3-dibromopropylamine hydrobromide and 0.1 mole of thiourea was dissolved in 70 ml of anhydrous isoamyl alcohol* with heating and then the solution was heated under reflux with stirring for 2–4 hr. The obtained precipitate was filtered and then separated from ammonium bromide by recrystallization from a mixture of ethyl acetate and methanol (1:1), and then from a mixture of methanol and propanol (1:1). The compounds were also identified as the picrates, which were obtained as precipitates when the compounds were treated with aqueous picric acid solution.

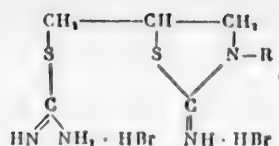
All of the obtained thiazolidines are white crystalline compounds, readily soluble in water and hot methanol, and insoluble in ether, acetone, and chloroform. The properties of the compounds are given in Table 3.

SUMMARY

1. Experimental proof was obtained for the earlier expressed theory that the dihydrobromide of 2-amino-5-isothiuroniummethylthiazoline is formed when thiourea is reacted with the hydrobromide of 2,3-dibromopropylamine.

2. It was shown that cyclization also takes place when thiourea is reacted with the hydrobromides of N-alkyl-2,3-dibromopropylamines, with the formation of the corresponding 2-imino-3-alkyl-5-isothiuroniummethylthiazolidines.

* Anhydrous isobutyl alcohol was used in the case of N-ethyl-2,3-dibromopropylamine.



Calculated %				M. p. of picrate	Analysis data for picrates					
					found %		Empirical formula	calculated %		
C	H	N	Br		C	H		C	H	
22.12	4.23	14.73	42.05	216°	33.60, 33.70	3.09, 3.18	C ₁₉ H ₂₀ O ₁₄ N ₁₀ S ₂	33.74	3.00	
24.38	4.60	14.21	40.55	223	34.55, 34.62	3.29, 3.32	C ₂₀ H ₂₂ O ₁₄ N ₁₀ S ₂	34.80	3.21	
26.48	4.92	13.41	39.15	240—241	35.76, 35.81	3.67, 3.70	C ₂₁ H ₂₄ O ₁₄ N ₁₀ S ₂	35.78	3.43	
28.44	5.14	13.26	37.84	249	36.58, 36.44	3.79, 3.69	C ₂₂ H ₂₆ O ₁₄ N ₁₀ S ₂	36.93	3.66	
28.44	5.14	13.26	37.84	240	36.89, 36.87	3.74, 3.92	C ₂₂ H ₂₆ O ₁₄ N ₁₀ S ₂	36.93	3.66	

3. Five new S-substituted thiourea derivatives—the dihydrobromides of 2-imino-3-alkyl-5-isothlurionium-methylthiazolidines—were synthesized.

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REACTION OF MERCURIC MONOCHLOROACETATE AND BENZOATE WITH PEROXIDES

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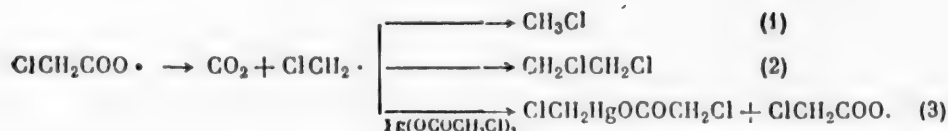
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Earlier we had shown that mercuric acetate [1, 2] and propionate [3] undergo chain free-radical decarboxylation when reacted with peroxides with the formation of alkylmercury salts. The n-nonylmercury salt was obtained from mercuric decanoate and decanoyl peroxide [4], but here the reaction did not have a chain character. It seemed of interest to determine whether similar processes would take place in the case of the mercury salts of substituted aliphatic acids, on the one hand, and of aromatic acids, on the other. For this purpose we studied the reaction of mercuric monochloroacetate with benzoyl and monochloroacetyl peroxides and of mercuric benzoate with benzoyl peroxide.

When mercuric monochloroacetate was reacted with monochloroacetyl peroxide in benzene we obtained a small amount of the monochloromethylmercury salt. At the same time the phenylmercury salt was obtained in 45.0%. In addition, the reaction mixture contained mercurous monochloroacetate, unreacted mercuric salt, free monochloroacetic acid and dichloroethane. The gas was found to contain CO₂, CO and methyl chloride.

In the case of reacting benzoyl peroxide with mercuric monochloroacetate in benzene the chloromethylmercury salt was not obtained. Here we obtained the phenylmercury salt, the yield of which increased with increase in the amount of peroxide taken. In addition, the reaction mixture contained mercurous monochloroacetate, unreacted mercuric salt, traces of metallic mercury, biphenyl, benzoic acid and monochloroacetic acid. The gas contained CO₂ and traces of CO.

On the basis of the obtained data it is possible to theorize that in the case of monochloroacetyl peroxide a decarboxylation of the chloroacetoxy radical, formed in the thermal decomposition of the peroxide, took place. The obtained chloromethyl radical reacted in three directions: it cleaved hydrogen, forming methyl chloride, it dimerized to dichloroethane, and it also entered into radical-substitution reaction with the mercuric monochloroacetate, giving the chloromethylmercury salt.



The last reaction is not chain in character, since the formation of chloromethyl compounds of mercury was not observed in the reaction with benzoyl peroxide. The formation of the phenylmercury salt in the reaction with monochloroacetyl peroxide can be explained only by a mercuration of the benzene by the mercuric monochloroacetate. Actually, the phenylmercury salt was isolated in substantial yield when mercuric monochloroacetate was reacted with benzene in the absence of peroxides. With benzoyl peroxide the formation of the phenylmercury salt can occur both as the result of benzene mercuration and because of replacement of the chloroacetoxy radi-

cal of the salt by the phenyl radical from the peroxide. That the last reaction takes place is shown by the fact that the yield of phenylmercury salt is increased when the amount of benzoyl peroxide taken for reaction is increased.

The reaction of mercuric benzoate with benzoyl peroxide in benzene had been studied by us earlier [5]; the formation of small amounts of phenylmercury salt was observed here. We were unable to determine whether the phenylmercury salt was formed as the result of reaction between peroxide and mercuric benzoate or because of mercuration of the benzene. To obtain an answer here, we employed *n*-octane and carbon tetrachloride as the reaction medium in the present paper. In both solvents the mercuric benzoate failed to react with the benzoyl peroxide and was recovered unchanged. In the case of *n*-octane we found benzene and benzoic acid in the solution, while in the case of carbon tetrachloride we isolated chlorobenzene and benzoic acid from the reaction. In addition, we observed that hexachloroethane was formed in CCl_4 medium. In both cases the gas contained CO_2 and traces of CO. In general the formation of these products corresponds with the results obtained in [6-8].

The mercuration of benzene when it was refluxed with mercuric benzoate could not be detected.

EXPERIMENTAL

Mercuric monochloroacetate was prepared from sodium monochloroacetate and analytically pure mercuric nitrate; m.p. 133-140°.

Found %: Hg 51.48, 51.71. $\text{C}_4\text{H}_4\text{O}_4\text{Cl}_2\text{Hg}$. Calculated %: Hg 51.8.

Mercuric benzoate was prepared from sodium benzoate and analytically pure mercuric nitrate. Monochloroacetyl chloride was obtained by the method of [9]; b.p. 104-104.5 at 730 mm; n_D^{20} 1.4540. Monochloroacetyl peroxide was synthesized from monochloroacetyl chloride by the modified Vanino method [10, 11]; the crude peroxide was dissolved in benzene and the solution was dried over CaCl_2 ; the amount of peroxide in the solution was determined iodometrically just prior to each experiment. Benzoyl peroxide was prepared and purified by the method of [12]. The thiophene-free benzene was distilled from sodium. "Pure" normal octane was distilled from sodium; b. p. 125° at 748 mm; unsaturated compounds were absent; n_D^{20} 1.3975. The carbon tetrachloride was freed of sulfur and then fractionally distilled, b.p. 76.5°. The reactions were run in the earlier described apparatus [1]. A VTI-2 gas analyzer and a Kh-1M chromatographic gas analyzer were used to analyze the gas.

Reaction of mercuric monochloroacetate with monochloroacetyl peroxide in benzene at 80°. A benzene solution (52 ml) of monochloroacetyl peroxide, containing 9.5 g (0.051 mole) of pure peroxide, was added in 30 min to a heated mixture of 11.65 g (0.03 mole) of mercuric monochloroacetate and 70 ml of benzene. The heating and stirring was continued for 2 hr. The collected gas analyzed 2020 ml (0.0902 mole) of CO_2 and 12.7 ml (0.00057 mole) of CO. The reaction mass was filtered to give 1.09 g of a precipitate, which proved to be mercurous monochloroacetate (tests with NH_4OH , KCl, and KI); the yield was 12.35%. The filtrate was treated with KCl, and the benzene was distilled from the mixture. The residue was treated with hot water, and the solution was found to contain 4.85 g of free monochloroacetic acid. Then the solution was extracted with ether, and the extract was dried over CaCl_2 and then evaporated to dryness. The residue was recrystallized from alcohol, and then from petroleum ether; weight 0.05 g, m.p. 130°, which corresponds to ClCH_2HgCl ; yield 0.58%. The portion insoluble in hot water was steam-distilled. The still residue was filtered from the precipitate, which after recrystallization from acetone gave 4.22 g of phenylmercury chloride, m.p. 252°; the mixed melting point with the pure substance was not depressed. Yield 45.0%. Treatment of the filtrate and of the ether-extracted solution with H_2S gave 2.82 g of HgS ; yield 40.4%.

We isolated 2.32 g of oil from the steam distillate, which was dried and then distilled, b.p. 145-149° at 21 mm. The distillate had b.p. 253.5° at 740 mm (according to Sivolobov), and n_D^{20} 1.5331. Analysis gave in %: C 64.04, 64.11; H 5.35, 5.79; Cl 18.14, 18.16. Isothiuronium picrate, m.p. 218-220°. The test for mercury was negative. The substance was not investigated further. The benzene that was distilled from the reaction mass was refluxed with 0.5 g of thiourea. Then the benzene was removed by distillation, while the residue was dissolved in alcohol and treated with picric acid. We obtained about 0.9 g of isothiuronium picrate with m.p. 250° (corr.); the mixed melting point with the isothiuronium picrate prepared from 1,2-dichloroethane was not depressed.

In a separate experiment the evolved gas, before entering the gas buret, was passed through an ice-water cooled wash bottle, containing 15 ml of alcohol. The flask contents were treated with thiourea and picric acid. We obtained about 0.45 g of *S*-methylisothiuronium picrate with m.p. 221.5° (corr.); the mixed melting point

with the S-methylisothiuronium picrate prepared from methyl iodide was not depressed.

Reaction of mercuric monochloroacetate with benzoyl peroxide in benzene at 80°. A solution of 2.47 g (0.01 mole, calculated as 100%) of benzoyl peroxide in 40 ml of benzene was added to a heated mixture of 11.65 g (0.03 mole) of mercuric monochloroacetate and 60 ml of benzene, after which the mixture was heated and stirred for 12 hr. The evolved gas contained 400 ml (0.0179 mole) of CO₂. The reaction mass was investigated in the same manner as described above. We isolated 2.73 g of mercurous monochloroacetate (30.9%), 0.59 g of HgS (8.45%), 5.62 g of phenylmercury chloride (59.9%), 0.48 g of biphenyl and 0.43 g of benzoic acid. Titration revealed that the yield of free monochloroacetic acid was 1.29 g. Chloromethylmercury compounds were not found.

In a second experiment we used 4.94 g (0.02 mole) of benzoyl peroxide. The gas analyzed 821 ml (0.0367 mole) of CO₂ and 4.0 ml (0.00018 mole) of CO. We isolated 6.42 g of phenylmercury chloride (68.4%) and 0.62 g (8.88%) of HgS from the reaction mass. The yield of mercurous salt was 20.95% (determined as mercurous chloride, weight 1.49 g). We also obtained 1.07 g of biphenyl and 0.98 g of benzoic acid. The amount of free monochloroacetic acid was 1.52 g. Traces of metallic mercury were detected. Chloromethylmercury compounds were not found.

Mercuration of benzene with mercuric monochloroacetate at 80°. A mixture of 11.65 g (0.03 mole) of mercuric monochloroacetate and 100 ml of benzene was heated under reflux with stirring for 12 hr. Gas evolution was not observed. Using the above described procedure, we isolated from the reaction mass 1.52 g (17.2%) of mercurous monochloroacetate, 2.06 g (21.9%) of phenylmercury chloride and 4.17 g (59.7%) of HgS. Traces of metallic mercury were also detected.

Reaction of mercuric benzoate with benzoyl peroxide in n-octane at 97–98°. Benzoyl peroxide (7.41 g; 0.03 mole, calculated as 100%) was added to a heated mixture of 13.28 g (0.03 mole) of mercuric benzoate in 100 ml of n-octane. The heating and stirring of the mixture was continued for 4 hr. The evolved gas analyzed 913 ml (0.0408 mole) of CO₂ and traces of CO. The reaction mass was filtered to give 12.94 g of a precipitate, which proved to be mercuric benzoate (97.5% of the original amount). The solvent was distilled from the filtrate in vacuo; the distillate contained a trace amount of unsaturated compounds. The residue was treated with KCl, and then steam was passed through the mixture. The residue from the steam distillation was filtered; the precipitate failed to contain phenylmercury compounds. The filtrate was treated with H₂S to give 0.04 g of HgS; yield 0.57%. We isolated 1.26 g of benzoic acid from the steam distillate; m.p. 121° (from water); the mixed melting point with the pure substance was not depressed.

In a separate experiment about 15 ml of distillate was removed from the n-octane solution, after which the distillate was dissolved in CCl₄ and nitrated. We obtained about 3 g of m-dinitrobenzene with m.p. 89° (from methanol); the mixed melting point with the pure substance was not depressed; an acetone solution of the compound gave a violet color with KOH.

Reaction of mercuric benzoate with benzoyl peroxide in carbon tetrachloride at 76°. A solution of 4.94 g (0.02 mole, calculated as 100%) of benzoyl peroxide in 20 ml of CCl₄ was added to a heated mixture of 13.28 g (0.03 mole) of mercuric benzoate in 80 ml of CCl₄. The heating and stirring of the mixture was continued for 12 hr. The evolved gas analyzed 562 ml (0.0251 mole) of CO₂ and 5.4 ml (0.00024 mole) of CO. The reaction mass was filtered to give 13.13 g of a precipitate, which proved to be mercuric benzoate (98.9% of the original amount). The solvent was distilled from the filtrate, and the distillate was nitrated. We obtained the β-form of 2,4-dinitrochlorobenzene with m.p. 43°; the mixed melting point with the substance prepared by the nitration of chlorobenzene in CCl₄ solution was not depressed. The residue after distilling off the solvent was investigated by the above described procedure. We obtained 2.03 g of hexachloroethane with m.p. 182° (in a sealed capillary) and 0.22 g of benzoic acid, m.p. 121° (from water); the mixed melting point with the pure substance was not depressed. Phenylmercury compounds were not detected.

Mercuration of benzene with mercuric benzoate at 80°. A mixture of 13.28 g (0.03 mole) of mercuric benzoate and 100 ml of benzene was heated and stirred for 12 hr. Gas evolution was not observed. The reaction mass was filtered to give 13.23 g of unreacted mercuric benzoate (99.6% of that taken). Traces of the mercuric salt were isolated from the filtrate as HgS. Phenylmercury compounds and benzoic acid were not found.

SUMMARY

1. The chain decarboxylation of the salt was not observed when mercuric monochloroacetate was reacted with monochloroacetyl and benzoyl peroxides.

2. The formation of trace amounts of chloromethylmercury salt was observed when mercuric monochloroacetate was reacted with monochloroacetyl peroxide in benzene. Here the benzene was mercurated with the formation of the phenylmercury salt. In addition, the other reaction products were the mercurous salt, monochloroacetic acid, methyl chloride, dichloroethane, CO_2 and CO .

3. The phenylmercury salt, the mercurous salt, biphenyl, benzoic acid, monochloroacetic acid, CO_2 and CO were isolated.

4. Mercuric benzoate in n-octane or carbon tetrachloride does not react with benzoyl peroxide; only the products of the reaction of the peroxide with the solvent were found here.

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SYNTHESIS AND STUDY OF SOME ACRIDINE COMPOUNDS AND THEIR N-OXIDES. I.

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It is known that many acridine compounds are physiologically active and some of them possess weak anti-virus action [1], as, for example, proflavine [2], tryptaflavine [3] and 2-nitro-5-aminoacridine [4]. In this connection it seemed of interest to synthesize a number of acridine compounds and test them on viruses, in particular, on the poliomyelitis virus, and also to study their chemical properties. Special attention was given to the N-oxides of the acridine series.

The N-oxides of the acridine series were obtained by the generally known procedure—the oxidation of the corresponding acridine bases with perbenzoic acid in chloroform solution [5, 6]. The acridine compounds having the aliphatic groupings: 2-hydroxy-3-diethylaminopropylamino and 3-diethylamino-2-methylbutylamino in the 9 position were synthesized from the corresponding 9-chloro or 9-phenoxy derivatives and aliphatic amines by heating their mixture in phenol medium. The N-oxides of the acridine compounds containing 9-alkylaminoalkyl radicals were not obtained by the oxidation of these bases, but instead they were obtained by reacting the N-oxides of the corresponding 9-phenoxy derivatives with aliphatic amines in phenol medium. The properties of the compounds, previously unknown in the literature, are given in the table (see footnote to the table).

Nearly all of the synthesized acridine bases are high melting crystalline compounds, colored either yellow or red, difficultly soluble in water, and moderately soluble in alcohol or benzene. The N-oxides of the acridine bases are also high melting crystalline compounds, having, as a rule, a deeper color than the starting bases. All of these compounds, both the unoxidized acridine bases and the N-oxides, are capable of forming hydrochlorides, which are colored yellow and are fairly soluble in water.

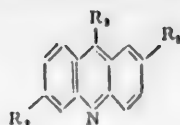
The results of the biological testing will be published in a separate communication.

EXPERIMENTAL

9-(3'-Diethylamino-2'-hydroxypropyl) aminoacridine dihydrochloride (I). 3-Diethylamino-2-hydroxypropylamine (1.2 g) was added to a hot solution of 2.2 g of phenoxyacridine in 3.5 g of phenol. The reaction mass was heated on the boiling water bath for 40 min, then cooled, and treated with 50 ml of ether. The ether solution was washed in a separatory funnel with 100 ml of 10% aqueous NaOH solution. The excess ether was evaporated, while the residue, a yellow compound, was recrystallized from anhydrous benzene. Weight 1.4 g (52%), m.p. 94°.

The free base was dissolved in anhydrous benzene. The benzene solution was saturated with dry hydrogen chloride under cooling. The hydrochloride deposited as an oil, which crystallized on standing and rubbing with a glass rod.

Synthesized Compounds



No. of compound	Values of R_1 , R_2 , and R_3	Melting point, recrystallization solvent, and color of compound	Yield (in %)	Empirical formula	Analysis results, in % (the calculated values are given in parentheses)		
					C	H	N
I	$R_1 = H, R_2 = H,$ $R_3 = -NHCH_2CH(OH)CH_2N(C_6H_5)_2$ Dihydrochloride	242–246° Acidified anhydrous methyl alcohol Yellow-green	58.3	$C_{27}H_{27}ON_3Cl$	60.35 (60.35)	6.70 (6.80)	10.55 (10.60)
II	$R_1 = -OCH_3, R_2 = H,$ $R_3 = -NHCH_2CH(OH)CH_2N(C_6H_5)_2$ Dihydrochloride	239–240° Anhydrous methyl alcohol and ether Bright yellow	25.0	$C_{21}H_{21}ON_3Cl$	58.69 (59.10)	6.74 (6.80)	10.10 (9.86)
III	$R_1 = H, R_2 = Cl,$ $R_3 = -NHCH_2CH(OH)CH_2N(C_6H_5)_2$ Dihydrochloride	135–136° Aqueous alcohol Yellow	31.4	$C_{20}H_{17}N_3OCl$	67.49 (67.13)	6.63 (6.71)	12.16 (11.75)
IV	$R_1 = H, R_2 = Cl, R_3 = Cl$ N-Oxide	167–168° Ethyl methyl ketone Orange	49.8	$C_{11}H_{11}ONCl$	58.81 (59.31)	2.73 (2.66)	5.64 (5.32)
V	$R_1 = H, R_2 = Cl, R_3 = -OC_6H_5$ N-Oxide	150–151° Anhydrous alcohol and pyridine Orange-red	51.0	$C_{11}H_{11}O_2NCl$	70.93 (70.91)	3.83 (3.73)	4.56 (4.36)
VI	$R_1 = -OC_6H_5, R_2 = NO_2,$ $R_3 = -OC_6H_5$ N-Oxide	155° Alcohol and benzene Deep red	38.0	$C_{11}H_{11}O_2N_2$	67.35 (67.05)	4.54 (4.25)	7.37 (7.44)
VII	$R_1 = H, R_2 = H,$ $R_3 = -NHCH_2CH(CH_3)CH_2N(C_6H_5)_2$ N-Oxide trihydrochloride	162–178° (decompn.) Acidified methyl alcohol Bright yellow	49.4	$C_{21}H_{23}ON_3Cl_3$	57.62 (57.3)	6.95 (6.98)	9.15 (9.12)
VIII	$R_1 = H, R_2 = H,$ $R_3 = -NHCH_2CH(OH)CH_2N(C_6H_5)_2$ N-Oxide dihydrochloride	225° Acidified methyl alcohol Bright yellow	43.9	$C_{20}H_{21}O_2N_3Cl_2$	58.13 (58.20)	6.55 (6.55)	10.80 (10.18)
IX	$R_1 = H, R_2 = Cl,$ $R_3 = -NHCH_2CH(OH)CH_2N(C_6H_5)_2$ N-Oxide dihydrochloride	243–244° Acidified anhydrous methyl alcohol Lemon yellow	28.7	$C_{22}H_{21}O_2N_3Cl_2$	53.37 (53.67)	5.87 (5.82)	9.49 (9.40)

No. of compound	Values of R ₁ , R ₂ , and R ₃	Melting point, recrystallization solvent, and color of compound	Yield (in %)	Empirical formula	Analysis results, in % (the calculated values are given in parentheses)		
					C	H	N
X	$R_1 = -OCH_3$, $R_2 = Cl$, $R_3 = -NHCH_2CH(OH)CH_2N(C_2H_5)_2$ N-Oxide dihydrochloride	235—236° (decompn.) Acidified methyl alcohol Yellow	73.0	$C_{21}H_{29}O_3N_2Cl_2$	61.91 (52.80)	5.71 (5.80)	8.84 (8.80)

Remarks. Compound (I) is known in the literature. We obtained it with m. p. 242—246° (decompn.), in contrast to the m. p. of 230° (decompn.) given in the literature [7, 8].

6-Chloro-9-(3'-diethylamino-2'-hydroxypropyl)aminoacridine (III) was synthesized in a similar manner.

6-Chloro-9-phenoxyacridine N-oxide (V). A solution of 1.5 g of 6-chloro-9-phenoxyacridine N-oxide in 30 ml of chloroform was treated with a chloroform solution containing 0.82 g of perbenzoic acid. After standing for 5 hr at room temperature the dark red solution was evaporated to dryness; the residue was treated with 5% NH_4OH . The precipitate was washed with ether and recrystallized first from a mixture of anhydrous alcohol and pyridine (3:1), and then from anhydrous alcohol.

6,9-Dichloroacridine N-oxide (IV) and 2-ethoxy-6-nitro-9-phenoxyacridine N-oxide (VI) were synthesized in exactly the same manner.

9-(3'-Diethylamino-2'-methylbutyl)aminoacridine N-oxide trihydrochloride (VII). One gram of 9-phenoxyacridine N-oxide was fused with phenol and the obtained melt was treated with 0.6 g of diethylamino-methylbutylamine. The reaction mass was heated for 30 min on the water bath, after which it was cooled and poured into 150 ml of ether. The ether layer was washed with 2N NaOH solution. The residue from the evaporation of the ether was dried in a vacuum-desiccator. Here the red oily liquid crystallized. The obtained free base, m.p. 80°, was dissolved in anhydrous benzene. Then the solution was treated with a saturated benzene solution of dry hydrogen chloride, which gave the hydrochloride as a precipitate.

9-(3'-Diethylamino-2'-hydroxypropyl) aminoacridine N-oxide dihydrochloride (VIII). A mixture of 1.5 g of 9-phenoxyacridine N-oxide, 3.0 g of phenol and 0.75 of 3-diethylamino-2-hydroxypropylamine was heated for 30 min on the boiling water bath. On conclusion of reaction the reaction mass was cooled and poured into 150 ml of absolute ether. The obtained dark red precipitate was filtered and then washed several times with ether to remove traces of phenol. The obtained free base was then allowed to stand for a day with a saturated absolute ether solution of dry hydrogen chloride.

6-Chloro-9-(3'-diethylamino-2'-hydroxypropyl) aminoacridine N-oxide dihydrochloride (IX). A mixture of 1 g of 6-chloro-9-phenoxyacridine and 1.52 g of 2-hydroxy-3-diethylaminopropylamine was heated on the water bath for 3 hr. The dark Bordeaux melt was poured into 200 ml of ether. After drying in the air the product weighed 0.85 g (70.5%), and had m.p. 189—190°.

The free base was covered with 50 ml of anhydrous benzene, previously saturated with hydrogen chloride. Here we obtained 0.61 g of a bright yellow precipitate with m.p. 234°. After 3 recrystallizations from anhydrous alcohol we obtained 0.4 g of substance with m.p. 243—244°.

2-Methoxy-6-chloro-9-(3'-diethylamino-2'-hydroxypropyl) aminoacridine N-oxide dihydrochloride (X) was synthesized in a completely analogous manner.

2-Methoxy-9-(3'-diethylamino-2'-hydroxypropyl)aminoacridine dihydrochloride (II). Five grams of 2-methoxy-9-chloroacridine was melted with 20.0 g of phenol on the boiling water bath and then 5.0 g of 3-diethylamino-2-hy-

droxypropylamine was added to the obtained melt. After heating for 3 hr, the reaction mass was poured into absolutely dry ether. Here a yellow crystalline precipitate was obtained, which was filtered and treated with 1 N NaOH. The product was recrystallized from acetone. Weight 3.3 g (47.5%), m. p. 90-92°. The free base was covered with absolute ether, saturated with dry hydrogen chloride, and allowed to stand overnight at 0°.

SUMMARY

For purposes of biological testing we synthesized nine previously unknown 9-aminoacridine derivatives and N-oxides of the acridine series.

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THE POLAROGRAPHIC REDUCTION OF SOME DERIVATIVES OF ACRIDINE. II

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The literature contains examples of the action of certain acridine derivatives ("nitroacridine", "tryptaflavine", "proflavine" and others) on several forms of viruses (grippe, mumps, encephalitis and others) [1-3]. For biological tests on poliomyelitis virus we prepared a series of acridine derivatives, the synthesis of which was described in the previous communication [4]. In the present paper we present the results of a polarographic investigation of these acridine derivatives.

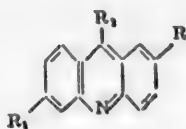
Of the compounds synthesized and tested only a few N-oxides of the acridine series possessed a weak virucidal action. Assuming that these substances have an oxidative action on viruses, we thought it would be interesting to carry out a comparative polarographic study of acridine N-oxides, thus making it possible to characterize quantitatively the reactivity of the N-O bond in compounds of different chemical structure. The complexity of the system of polarographic waves for the acridine derivatives necessitated a study of the reduction not only of the N-oxides but also of the corresponding unoxidized bases. Consequently 29 derivatives of acridine, of which 15 were N-oxides, were reduced polarographically.

Method of polarographic reduction and discussion of results. The polarographic investigation of the acridine derivatives was carried out with a photomicropolarograph using Heyrovsky's system. Measurements were made in acetate (pH 4.48) and ammonium (pH 9.25) buffers. The solvent was 96% alcohol from which traces of aldehydes and ketones were carefully removed. The concentration of the substances was 0.001 M. The half-wave potentials on the polarographic curves were determined by a graphical method.

Since it is known from literature data that acridine and most of its derivatives are reduced irreversibly at the dropping mercury electrode (Hg.d.e.), the number of electrons taking part in the reduction reaction cannot be calculated from the equation of the wave; nor can it be calculated from the Ilkovich equation because the diffusion coefficients for these compounds are not known. Hence when interpreting the polarograms obtained we can only speculate on the number of electrons participating in the reduction of our compounds on the basis of the heights of the polarographic waves as compared with that of unsubstituted acridine. In the case of the latter it is known with certainty that each wave corresponds to the addition of only one electron [5] (the concentrations of all the solutions tested were identical). The results obtained are presented in the table. The polarograms of several acridine derivatives are depicted in Figures 1 and 2.

The data indicate, as one would expect, that all the acridine derivatives tested were reduced at the Hg. d. e. Unsubstituted acridine (Table, substance 1 and Fig. 1, curve 1) in both the acetate and ammonium buffers gave two waves of identical height with $E_{1/2}$ -0.56 and -1.42 v; -0.86 and -1.40 v respectively. Data obtained for acridine [5] support the assumption that each stage of the reduction corresponds to the addition of only one atom of hydrogen, the first product of the reduction being the semiquinone, and the second acridan.

Results of Measurements of the Half-Wave Potentials of Derivatives of Acridine



(For each substance the measured value at pH 4.48 is given in the first line, and at pH 9.25 in the second line)

No.	Values of R, R ₁ and R ₂ in compounds	Half-wave potential v (n. c. e.) ^b		Limiting diffusion current, ma ^c	
		1st wave	2nd wave	1st wave	2nd wave
1	R = R ₁ = R ₂ = H	-0.56	-1.42	1.08	1.25
		-0.86	-1.40	1.25	1.25
2	N-Oxide	-0.80	—	3.66	—
	R = R ₁ = R ₂ = H	-1.02	—	3.48	—
3	R = R ₁ = H; R ₂ = Cl	-0.57	-1.42	3.50	1.33
		-0.76	-1.39	3.16	1.06
4	R = H; R ₁ = R ₂ = Cl	-0.51	Merged with back-ground	3.39	—
		-0.80	-1.28	3.50	1.06
5	R = OCH ₃ ; R ₁ = H; R ₂ = Cl	-0.71	-1.56	3.66	1.16
		-0.89	-1.47	3.66	1.28
6	R = OCH ₃ ; R ₁ = R ₂ = Cl	-0.58	-1.32	2.50	0.80
		-0.83	-1.42	3.92	1.04
7	R = OC ₂ H ₅ ; R ₁ = NO ₂ ; R ₂ = Cl	-0.29 ^a	-0.70	5.41	3.80
		-0.44 ^a	-0.90	4.16	3.75
8	N-Oxide	-0.75	-1.58	7.50	1.00
	R = R ₁ = H; R ₂ = Cl	-0.99	-1.59	5.83	1.04
9	N-Oxide	-0.70	-1.59	5.50	1.03
	R = H; R ₁ = R ₂ = Cl	-0.86	-1.44	5.33	1.20
10	N-Oxide	-0.76	-1.62	5.66	0.98
	R = OCH ₃ ; R ₁ = H; R ₂ = Cl	-0.96	-1.43	5.00	1.01
11	N-Oxide	-0.60	-1.20	4.83	0.83
	R = OCH ₃ ; R ₁ = R ₂ = Cl	-0.88	-1.35	4.90	1.33
12	N-Oxide	-0.28 ^a	-0.72	Waves very low, substance precipitated during measurement	
	R = OC ₂ H ₅ ; R ₁ = NO ₂ ; R ₂ = Cl	-0.44 ^a	-0.88		
13	R = R ₁ = H; R ₂ = OC ₆ H ₅	-0.66	-1.48	1.33	4.16
		-0.92	-1.44	1.00	2.66
14	R = H; R ₁ = Cl; R ₂ = OC ₆ H ₅	-0.63	-1.46	1.01	3.16
		-0.88	-1.42	1.50	3.33
15	R = OCH ₃ ; R ₁ = H; R ₂ = OC ₆ H ₅	-0.75	-1.52	1.02	3.05
		-0.04	-1.55	0.92	3.15
16	R = OCH ₃ ; R ₁ = Cl; R ₂ = OC ₆ H ₅	-0.64	-1.32	1.02	2.48
		-0.98	-1.42	1.05	3.15
17	N-Oxide	-0.79	Merged with back-ground	3.33	—
	R = R ₁ = H; R ₂ = OC ₆ H ₅	-1.00	-1.49	3.33	3.00

(Continuation)

No.	Values of R, R ₁ and R ₂ in compounds	Half-wave potential v (n. c. e.) ^b		Limiting diffusion current, ma ^c	
		1st wave	2nd wave	1st wave	2nd wave
18	N-Oxide R = H; R ₁ = Cl; R ₂ = OC ₆ H ₅	-0.71 -0.91	-1.48 -1.40	3.33 3.35	3.16 2.96
19	N-Oxide R = OCH ₃ ; R ₁ = H; R ₂ = OC ₆ H ₅	-0.69 -0.97	-1.32 -1.38	2.70 3.38	3.05 2.91
20	N-Oxide R = OC ₆ H ₅ ; R ₁ = Cl; R ₂ = OC ₆ H ₅	-0.66 -0.86	-1.32 -1.29	2.81 2.81	2.64 2.50
21	N-Oxide R = OC ₂ H ₅ ; R ₁ = NO ₂ ; R ₂ = OC ₆ H ₅	-0.24* -0.44*	-0.78 -1.09	3.18 3.41	3.18 3.38
22	R = R ₁ = H; R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-1.05 -1.07	-1.32 -1.42	— 0.91	— 3.16
23	R = H; R ₁ = Cl R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-0.87 -0.97	-1.17 -1.30	1.00 0.91	2.91 2.66
24	R = OCH ₃ ; R ₁ = H R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-1.00 -1.01	-1.26 -1.29	1.01 0.98	2.33 3.15
25	R = OCH ₃ ; R ₁ = Cl R ₂ = NHCH ₂ CHNHCN(C ₂ H ₅) ₂ Dihydrochloride	-0.89 -1.04	-1.20 -1.39	1.03 0.91	3.33 3.16
26	N-Oxide R = R ₁ = H; R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-1.11 -1.12	— -1.45	6.66 1.03	— 2.66
27	N-Oxide R = H; R ₁ = Cl; R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-0.84 -1.03	-1.16 -1.31	2.56 2.66	2.66 2.66
28	N-Oxide R = OCH ₃ ; R ₁ = H R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-1.05 -1.02	— -1.32	5.83 2.83	— 2.83
29	N-Oxide R = OCH ₃ ; R ₁ = Cl R ₂ = NHCH ₂ CHOHCH ₂ N(C ₂ H ₅) ₂ Dihydrochloride	-0.82 -1.01	-1.18 -1.28	2.50 2.50	2.66 2.83

a) This wave explained by reduction of nitro group.

b) 3rd wave: substance No. 7, at pH 4.48—merged with background, pH 9.25—1.29 v; substance No. 12, at pH 4.48 and 9.25—merged with background; substance No. 21 at pH 4.48 - 1.19 v, pH 9.25 - 1.47 v.

c) 3rd wave: substance No. 21 at pH 4.48—2.60 ma, pH 9.25—3.15 ma.

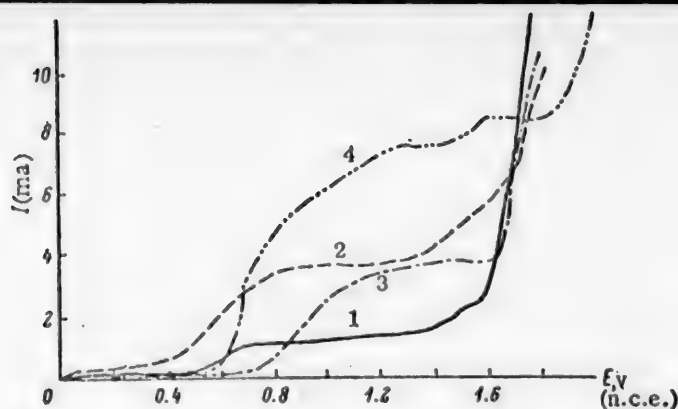
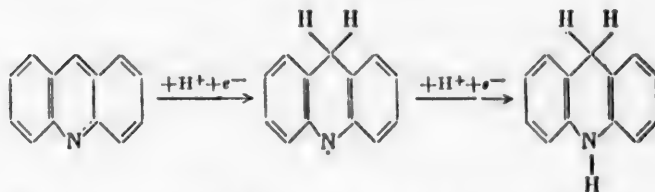
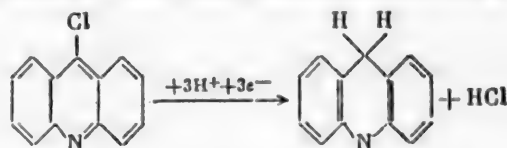


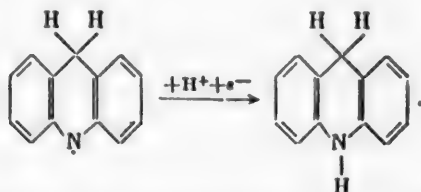
Fig. 1. Polarographic reduction curves for acridine derivatives in acetate buffer (pH 4.48). 1) Acridine; 2) acridine N-oxide; 3) 9-chloroacridine; 4) 9-chloroacridine N-oxide



From these data the approximate number of electrons can be determined which participate in the different stages of the reduction of the various acridine derivatives. In going from unsubstituted acridine to 9-chloroacridine (Table, substance 3 and Fig. 1, curve 3) the first wave increases to almost three times its height in unsubstituted acridine, with a break indicating the merging of two waves; the second wave has the same height and value of $E_{1/2}$ as the second wave in unsubstituted acridine. Analysis of the polarographic curve of 9-chloroacridine suggests that the reduction of this compound takes place in three stages; the first is dehalogenation of 9-chloroacridine, and then acridine is reduced to acridan in two stages. Since the half-wave potentials for the reduction of 9-chloroacridine and for the first stage in the reduction of acridine are very close, a wave is obtained on the polarogram corresponding to the addition of three atoms of hydrogen according to the following equation:



and a second low wave, corresponding to the final reduction of acridine—the semiquinone to acridan according to the equation:



Similar curves were obtained in the reduction of other derivatives of 9-chloroacridine (Table, substances 3-7).

Comparison of the polarographic reduction results for acridine and its N-oxide (Table, substances 1 and 2, Fig. 1, curves 1 and 2) shows that acridine N-oxide cannot give a wave due to reduction of acridine to the semiquinone because the first process—the reduction of oxide oxygen—takes place at a higher potential (-0.80 v) than the first stage in the reduction of acridine (-0.56 v). Consequently, by the time the reduction potential of acridine is reached it will no longer be present in the solution. Reduction of acridine begins together with the reduction of oxide oxygen, and the height of the wave will be determined by the number of electrons participating in both processes. If it be assumed that two electrons take part in the reduction of the N=O bond:

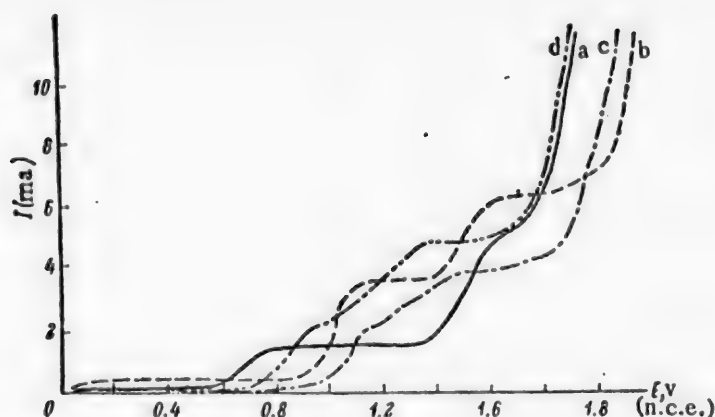
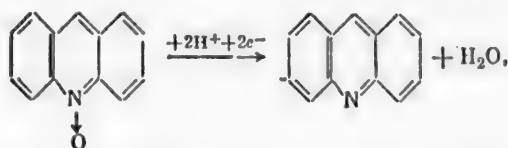


Fig. 2. Polarograms of acridine derivatives (pH 4.48).

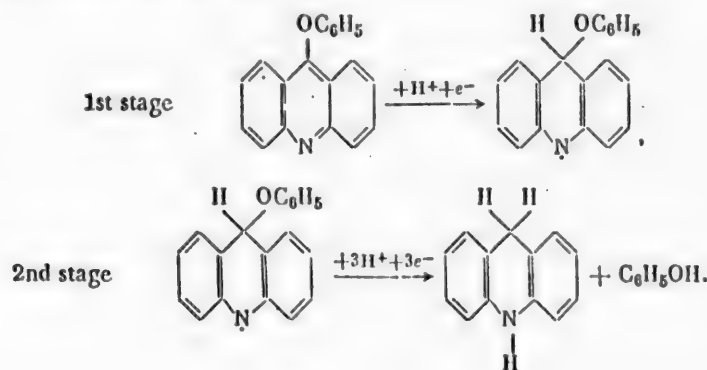
1) 9-Phenoxiacridine; 2) 9-phenoxiacridine N-oxide; 3) 9-(2-hydroxy-3-diethylaminopropylamino) acridine; 4) 9-(2-hydroxy-3-diethylaminopropylamino) acridine N-oxide.



and that the first stage in the reduction of acridine proceeds, as mentioned above, with one electron participating, then the height of the first wave of acridine N-oxide must be three times the height of the first wave of acridine. This agrees with the experimental data. [The maximum diffusion current (I_d) for the first wave of acridine N-oxide was 3.66 ma, and 1.08 ma for acridine].

In the case of the 9-chloroacridine N-oxides (Table, substances 8-12, Fig. 1, curve 4) three processes merge together: reduction of the N→O bond, dechlorination, and the first stage in the reduction of acridine; therefore on the polarograms of these compounds we see only two waves, the first of which is about five times the height of the second (I_d of the first wave varied from 4.83 to 7.50 ma and the second from 0.83 to 1.33 ma).

Interesting results were obtained in the polarographic reduction of acridine 9-phenoxy derivatives (Table, substances 13-16). All these compounds gave two waves on the polarograms: the first, a low one, corresponding to the addition of only one atom of hydrogen, and the second, $2\frac{1}{2}$ -3 times higher than the first, in the region of potential characteristic of the second stage in the reduction of acridine to acridan. Hence, the following course of the reduction of phenox compounds may be postulated:



The polarograms of the 9-phenoxyacridine N-oxides (Table, substances 17-21 and Fig. 2, curve 2) comprise two definite waves. The first wave is about three times as high as that of the unoxidized compound (Id increased from 1.33 for 9-phenoxyacridine to 3.33 ma for its N-oxide). All this undoubtedly indicates that here, as in the case of 9-chloroacridine N-oxides, the first wave is determined by the simultaneous reduction of the N-O bond and the first stage in the reduction of the acridine system.

Results of the polarographic reduction of 9-(2-hydroxy-3-diethylaminopropylamino) acridines are given in the table under Nos. 22-25, and the polarogram of the reduction of 9-(2-hydroxy-3-diethylpropylamino) acridine is shown in Fig. 2, curve 3. The polarograms of this group of compounds have the same character as the reduction curves of the corresponding 9-phenoxy compounds: two similar waves are observed on the polarogram—the first low and the second high, which indicates that the course of the reduction is the same for these compounds. However, in the case of the 9-alkylaminoacridines the half-wave potential of the first wave has a more negative value ($E_{1/2}$ varied from -0.89 to -1.05 v in the acetate buffer). This fact supports the view that introducing an alkylamino group into position 9 of the acridine system inhibits markedly the reduction of the latter.

As would be expected, with the N-oxides of 9-(2-hydroxy-3-diethylaminopropylamino) acridines (Table, substances 26-29 and Fig. 2, curve 4) the character of polarograms of the corresponding unoxidized compounds was retained, but the height of the first wave increased approximately three times.

Thus analysis of the data obtained shows that: 1) Introduction of different types of substituents (chloro, methoxy, nitro, phenoxy groups) into the 2, 6 and 9 positions of acridine has essentially no influence on its reducibility at the Hg.d.e. An exception is the introduction of an alkylamino group into position 9, which inhibits markedly the reduction of the acridine system. (In going from unsubstituted acridine to its 9-alkylamino analog the half-wave potential changed from -0.56 to -1.05 v in the acetate buffer and from -0.86 to -1.07 v in the ammonium buffer). In this connection it is interesting to recall that previously [5] a definite relationship was established between the reducibility of aminoacridines at the Hg.d.e. and their biological activity. Thus, it was observed that the acridines which are the most difficult to reduce are also the most biologically active compounds. The results obtained with our compounds are in complete agreement with this conclusion, because active antimicrobial substances with a wide spectrum of antibacterial action were found only among the 9-alkylaminoacridines which were the most difficult to reduce.

2) On the other hand, the data obtained indicate that the virucidal properties of acridine N-oxides are connected to some extent with the oxidizing properties of the latter, because the only compounds among those tested which had a weak action on poliomyelitis virus were N-oxides of certain 9-alkylaminoacridines (Table, substances 10 and 11) which were most easily reduced. However, in view of the merging together of the reduction of the N-O bond and the first stage in the reduction of the acridine system, and also in view of the lack of sufficient experimental material, it is impossible to draw definite conclusions regarding the relationship between the chemical structure of acridine N-oxides and their virucidal properties.

3) It may also be concluded from the data cited that the values of the half-wave potentials of the first stage in the reduction of acridine derivatives are dependent to a large extent upon the acidity of the medium (thus, with unsubstituted acridine $E_{1/2}$ changed from -0.56 to -0.86 v when the pH increased from 4.48 to 9.25), while the second stage in the reduction of the acridine system is almost independent of the pH of the medium.

Finally we should like to express our deep thanks to L. G. Perets and O. V. Bichkovskii, and also to co-workers in the immunobiological laboratory at the Sverdlovsk Poliomyelitis Prophylaxis Research Institute for carrying out biological tests on the acridine series of compounds which we prepared.

SUMMARY

1. Twenty-nine derivatives of acridine were reduced polarographically.
2. The biological activity (antibacterial and virucidal action) of the acridine series of compounds appears to depend to a certain extent upon the reducibility at the dropping mercury electrode.

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THE SYNTHESIS OF UNSATURATED ESTERS OF DITHIOPHOSPHORIC ACIDS AND THEIR ACYL AND ALKYL DERIVATIVES*

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Esters of dithiophosphoric acids are insecticides and have several other fields of application [1]. However, only the saturated esters of these acids have been described, their synthesis being based usually on saturated alcohols and phosphorus pentasulfide [2-6]. Esters of unsaturated alcohols and dithiophosphoric acid have not been described in the literature.

With the object of studying them and of preparing new compounds of dithiophosphoric acid which might have insecticidal properties we synthesized O, O-diallyldithiophosphoric acid $(\text{CH}_2=\text{CH}-\text{CH}_2\text{O})_2\text{P}\begin{smallmatrix} \text{S} \\ \diagup \\ \text{SH} \end{smallmatrix}$ and some of its acyl and alkyl derivatives.

The allyl ester of dithiophosphoric acid was prepared by introducing allyl alcohol dropwise into a benzene suspension of freshly distilled phosphorus pentasulfide contained in a three-necked flask protected from moisture. The reaction began at a bath temperature of 50 °C and proceeded with the liberation of hydrogen sulfide.



The unreacted materials and solvent were removed and the oil (91-94.3%) which remained was purified by distillation at 10^{-4} mm.

The acid obtained was acylated and alkylated using acyl chlorides and alkyl halides in a benzene medium in the presence of triethylamine. The extent of the reaction was determined from the quantity of triethylammonium salt.

The derivatives were purified as described above for the acid, and studied. The results are presented in the table.

SUMMARY

- 1) The reaction between allyl alcohol and phosphorus pentasulfide was investigated. The diallyl ester of dithiophosphoric acid was prepared and studied.
- 2) Reactions were carried out between O, O-diallyldithiophosphoric acid and acyl chlorides corresponding to acetic, butyric, isovaleric, benzoic, oxalic, malonic, succinic, and glutaric acids, and the alkyl halides—iso-butyl bromide and isoamyl bromide—as the result of which the corresponding derivatives were prepared and studied.

* Ya. M. Borbulevich, N. E. Zhukov, and L. P. Pilipchuk participated in the experimental work.



Value of R	n_D^{20}	d_4^{20}	M_R		Molecular weight		Found (%)		Empirical formula	Calculated (%)		Yield (%)
			found	calculated	found	calculated	P	S		P	S	
(I), -H	1.5330	1.1656	55.99	56.00	204.0	210.2	14.69	30.08	$\text{C}_6\text{H}_{11}\text{O}_2\text{S}_2\text{P}$	14.73	30.50	94.3
(I), -COCH ₃	1.5470	1.2039	66.47	66.14	236.0	252.0	12.47, 12.39	24.78	$\text{C}_8\text{H}_{13}\text{O}_3\text{S}_2\text{P}$	12.28	25.41	85.0
(I), -COCH(CH ₃) ₂	1.5565	1.1877	75.66	75.37	261.0	280.0	11.10	22.55	$\text{C}_{10}\text{H}_{17}\text{O}_3\text{S}_2\text{P}$	11.05	22.87	80.5
(I), -COCH ₂ CH(CH ₃) ₂	1.5342	1.1519	79.45	79.99	304.0	294.0	10.51, 10.48	21.29	$\text{C}_{11}\text{H}_{19}\text{O}_3\text{S}_2\text{P}$	10.52	21.77	68.1
(I), -COC ₆ H ₅	1.5780	1.2121	86.13	85.65	308.0	314.36	10.16, 10.29	19.53	$\text{C}_{13}\text{H}_{15}\text{O}_3\text{S}_2\text{P}$	9.95	20.39	64.2
(II), -CO	1.5450	1.2454	120.33	120.83	455.0	474.0	13.28, 13.18	26.77	$\text{C}_{14}\text{H}_{20}\text{O}_6\text{S}_4\text{P}_2$	13.03	27.00	45.4
(II), -CO-CH ₂	1.5445	1.2205	126.31	125.45	464.0	488.0	12.49, 12.44	26.02	$\text{C}_{15}\text{H}_{22}\text{O}_6\text{S}_4\text{P}_2$	12.70	26.22	80.0
(II), -CO-CH ₂ -CH ₂	1.5440	1.2235	129.52	130.07	495.0	502.0	12.23, 12.29	25.38	$\text{C}_{16}\text{H}_{24}\text{O}_6\text{S}_4\text{P}_2$	12.35	25.49	50.0
(II), -CO-CH ₂ -CH ₂ -CH ₂	1.5432	1.2123	134.39	134.59	495.0	516.0	12.10, 12.01	24.57	$\text{C}_{17}\text{H}_{26}\text{O}_6\text{S}_4\text{P}_2$	12.01	24.80	60.0
(I), -CH ₂ CH(CH ₃) ₂	1.5254	1.1037	74.0	74.31	260.0	266.4	11.38	23.30	$\text{C}_{10}\text{H}_{19}\text{O}_2\text{S}_2\text{P}$	11.62	24.07	74.1
(I), -(CH ₂) ₂ CH(CH ₃) ₂	1.5238	1.0878	78.84	78.93	272.0	280.4	10.95	21.6	$\text{C}_{11}\text{H}_{21}\text{O}_2\text{S}_2\text{P}$	10.04	22.8	69.0

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THE UNIFORMITY OF ABIETINOL PREPARED BY THE METHOD
OF RUZICKA AND MEYER

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In 1922 Ruzicka and Meyer [1], while studying the structure of abietinic acid, prepared abietinol by the reduction of methyl abietinate. According to their data, abietinol was a liquid boiling at 169-172° C at 0.2 mm. A similar product was obtained using the same method in 1933 by Ruzicka and co-workers [2], and in 1953 by Le-Van Thol [3].

We obtained abietinol in the form of a crystalline compound with m.p. 85.5-86.5° C by reducing abietinic acid (from the resins of *Abies Sibirica* Ldb.) with lithium aluminum hydride. Its rotary dispersion coefficient, $\left(\frac{[\alpha]_F}{[\alpha]_C} = 2.16\right)$ was very close to that of abietinic acid (2.19). Its ultraviolet spectrum, like that of abietinic acid, contained a band with a maximum at 241 mμ.

These data convinced us that abietinol with m.p. 85.5-86.6° C is a single compound. The abietinol of Ruzicka and Meyer then required a more detailed investigation. We decided to reproduce the conditions employed by these authors in preparing abietinol and to explain the properties of their product by means of modern spectroscopic methods.

We isolated abietinic acid (m.p. 170-172° C $[\alpha]_D -102^\circ$ C) from the rosin of ordinary pine (*Pinus silvestris* L.) using Steele's method. This abietinic acid, and also that from Siberian fir, formed abietinol with m.p. 85.5-86.5° C when reduced with lithium aluminum hydride. Its p-nitrobenzoate melted at 130-130.5° C.

As the data cited in Table 1 show, our product was comparatively pure abietinic acid.

TABLE 1.

Properties of Abietinic Acid

Melting point	$[\alpha]_D$ in alcohol	λ_{max} in mμ	Specific absorption coefficient	Literature reference
170-172°	-102°	241	79.0 (lg ε 4.42)	In our experiments
174-175	-115.6	—	—	[5]
158	-68	—	—	[1]
170.2-172.7	-104	—	—	[6]
172-175	-106	241	77.0	[7]

TABLE 2

Properties of the Reduction Products of Methyl Abietinate

Boiling point (pressure in mm)	n_D^{20}	n_D^{25}	n_D^{30}	Literature reference
150—155° (0.05)	1.5487 (calculated)	1.5400	1.5391	In our experi- ments
169—172 (0.2)	1.5487	—	—	[1]

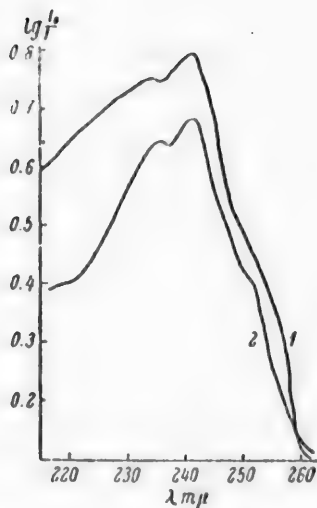


Fig. 1. Ultraviolet absorption spectra. 1) Abietinic acid; 2) methyl abietinate.

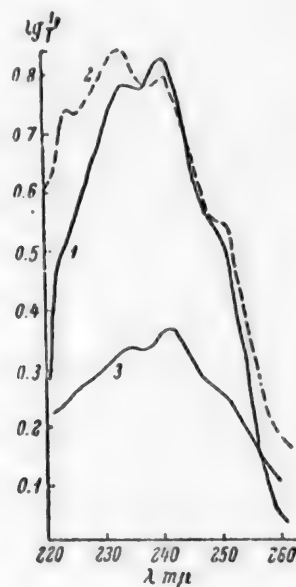


Fig. 2. Ultraviolet absorption spectra. 1) Abietinol; 2) product of reduction of methyl abietinate with sodium in anhydrous alcohol; 3) product with m.p. 63-65° C (Fraction 36-42° Table 3).

The properties of the methyl abietinate which we prepared were quite close to those of the methyl ester described by Ruzicka and Meyer [1]. Its ultraviolet spectrum contained the same band with a maximum at 241 mμ ($\lg \epsilon 4.22$) (see Fig. 1).

Reduction of the methyl ester with metallic sodium gave an alcohol similar in properties to the abietinol of Ruzicka and Meyer (Table 2).

However, a spectroscopic study showed considerable nonuniformity in the product (see Fig. 2). The spectrum of abietinol prepared by Ruzicka's method contains a band with two intense maxima; at 234 mμ ($\lg \epsilon 4.47$) and at 241 mμ ($\lg \epsilon 4.43$), the first maximum being more intense than the second, which is not observed in the spectrum of abietinol prepared by the reduction of abietinic acid with lithium aluminum hydride.

The infrared spectrum of abietinol prepared by Ruzicka's method differs somewhat from the spectrum of abietinol with m.p. 85.5-86.5°. In the spectrum of Ruzicka's abietinol there is a band of weak intensity at 1715 cm^{-1} , which indicates the presence of impurities containing the carbonyl group. Moreover, bands with maxima at 1295, 970 and 915 cm^{-1} had different intensities.

Not entirely satisfied with these results, we tried to purify chromatographically the abietinol product prepared by Ruzicka's method. By chromatography we succeeded in separating a product in the form of an amorphous powder with m.p. 63-65° C. The ultraviolet spectrum of this product (band with maximum at 241 mμ in Fig. 2) is similar to the spectrum of abietinol which we obtained by the reduction of abietinic acid with lithium

aluminum hydride. However, the intensity of the band is much less ($\log \epsilon 4.05$), which indicates the presence of impurities. Further purification of the product to give a more satisfactory result was not carried out.

All these data show that the product obtained by the reduction of methyl abietinate was not a pure compound. Apparently the prolonged heating with metallic sodium in an alcoholic medium gave rise to secondary reactions which resulted in contamination of the product.

EXPERIMENTAL

Abietinic acid was prepared according to Steele's method by boiling a solution of rosin (1180 g) in glacial acetic acid (900 g) for two hours. The resulting solution of isomerized rosin was filtered and allowed to stand in the cold for a day. After seven recrystallizations from alcohol 60 g of abietinic acid with m.p. 170-172°, $[\alpha]_D^{20} -102^\circ$ (c 2, alcohol) was obtained.

Methyl abietinate was prepared according to the directions of Ruzicka and Meyer [1] from silver abietinate and methyl iodide. Yield 36.3%. Boiling point 176-181° (0.1 mm), $n_D^{20} 1.5357$.

TABLE 3

Fraction No.	Eluant	Wt. of fraction (in mg)	Melting point
1-9	Petroleum ether + benzene (10:1)	30	Liquid
10-15	Petroleum ether + benzene (8:1)	—	—
16-22	Petroleum ether + benzene (5:1)	40	Liquid
23-27	Petroleum ether + benzene (2:1)	—	—
28-32	Petroleum ether + benzene (1:1)	—	—
33-35	Benzene	—	—
36-42	Petroleum ether + ethyl ether (1:1)	374	63-65°
43-50	Ethyl ether	30	Liquid

The reduction of methyl abietinate also was carried out according to the direction of Ruzicka and Meyer using metallic sodium in anhydrous alcohol [1]. The product weighed 1.62 g (44%) and boiled at 150-155° (0.05 mm).

Found %: C 83.05; H 11.06. $C_{20}H_{32}O$. Calculated %: C 83.27; H 11.18

Chromatographic treatment of the product. A solution containing 0.7 g of the reduction product of methyl abietinate in 10 ml of petroleum ether was introduced into a column filled with 90 g of alumina (neutral, Grade III activity as measured by Brockmann's method). Elution was carried out first with a mixture of petroleum ether and benzene, and then with a mixture of petroleum ether and diethyl ether. The filtrate was collected in 25 ml fractions. The chromatographic results are presented in Table 3.

The reduction of abietinic acid with lithium aluminum hydride was carried out as described in our previous communication [8]. The yield of abietinol was 92%, m.p. 85.5-86.5°, and $[\alpha]_D -132.5^\circ$ (c 2, alcohol).

Found %: C 83.47, 83.48; H 11.14, 11.07. Number of OH's 1.14, 1.09. $C_{20}H_{32}O$. Calculated %: C 83.27; H 11.18. Number of OH's 1.00.

p-Nitrobenzoate of abietinol. To a solution of 0.5 g of abietinol in 3 ml of pyridine was added 0.5 g of p-nitrobenzoyl chloride. The reaction mixture was heated on a water bath under reflux for two minutes. Then 10 ml of water was added to the reaction mixture with vigorous stirring. The precipitate was separated, treated with soda solution, filtered off, and recrystallized from alcohol. Yellowish, needle-shaped crystals were obtained weighing 0.47 g with m.p. 130-130.5°, and $[\alpha]_D -52.08^\circ$ (c 1.5, acetone).

Found %: C 73.59, 73.54; H 7.88, 7.84. $C_{27}H_{36}O_4N$. Calculated %: C 73.93; H 8.27.

SUMMARY

It was shown that abletinol obtained by reducing methyl abletinate with sodium in anhydrous alcohol is not a pure product.

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* Original Russian pagination. See C. R. translation.

THE REACTION OF SABINENE WITH PERACETIC ACID

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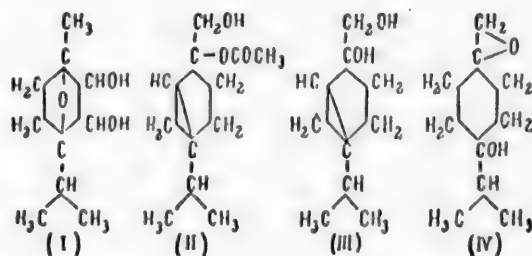
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An attempt to obtain sabinene oxide by the action of a solution of hydrogen peroxide in glacial acetic acid on sabinene has been described in the literature [1]. Two isomeric glycol anhydrides were separated out (I), one with m.p. 174°, $[\alpha]_D + 34.3^\circ$, the other with m.p. 172°, $[\alpha]_D \pm 0^\circ$, partly in a free state and partly in the form of acetic acid esters. In neither of these cases was the cyclopropane ring preserved. In addition to these products a small quantity of n-cymene was obtained.



The purpose of our investigation was to study the reaction of sabinene with peracetic acid. We did not succeed in obtaining sabinene oxide which, apparently, is an unstable compound that undergoes further change under the conditions of the reaction.

The basic product (63%) we obtained was sabineneglycol monoacetate (II). Its structure was established by saponification to the glycol (III) with b. p. 135 - 136° (6 mm), d_4^{20} 1.0228, n_D^{20} 1.4830. This glycol is apparently the stereoisomer of sabineneglycol described by Semmler [2] with a b. p. of 148 - 150° (15 mm), m.p. 54°, d_4^{20} 1.021, n_D^{20} 1.4802, which was obtained by the oxidation of sabinene by potassium permanganate. The oxidation of the glycol by means of lead tetraacetate gave sabinaketone which was identified by its semicarbazone with a m.p. of 139 - 140°.

The presence of the cyclopropane ring in molecules of sabineneglycol monoacetate and sabineneglycol is confirmed by the fact that the infrared spectra of these compounds shows a band with a maximum at 3062 cm^{-1} (Fig. 1), which, as is well known, is characteristic of the CH_2 -group of the cyclopropane ring [3].

The presence of a free primary alcohol group in the molecule of sabineneglycol monoacetate (II), in all probability, is indicated by a band in the infrared spectrum at 1044 cm^{-1} (Fig. 2). This band is also observed in the spectrum of sabineneglycol but is absent in the spectrum of sabinene.

The data of M. S. Malinovskii and A. G. Yudasina [4] give some confirmation that in the reaction of peracetic acid with sabinene it is precisely the tertiary alcohol group which is acetylated. These authors showed that in the reaction of perbenzoic acid with 2,2,3-trimethylbutene-3, the monobenzoate of the glycol is formed instead of the corresponding oxide; in the benzoate molecule a complex ester group is located at the tertiary carbon atom.

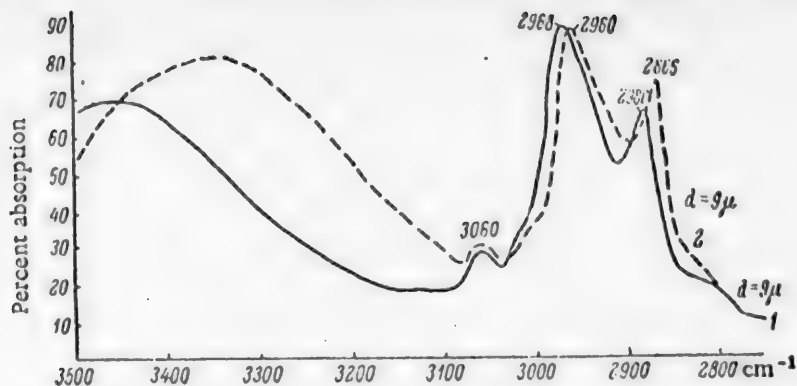


Fig. 1. Infrared absorption spectra in the region 2800 - 3500 cm^{-1} .
1) Sabineneglycol monoacetate; 2) sabineneglycol.

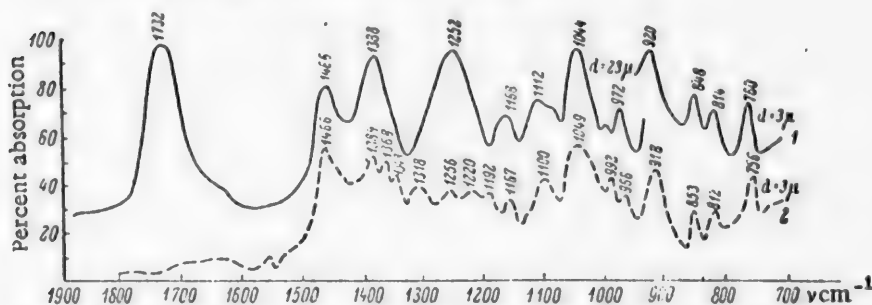


Fig. 2. Infrared absorption spectra in the region 700 - 1800 cm^{-1} .
1) Sabineneglycol monoacetate; 2) sabineneglycol.

Along with sabineneglycol monoacetate, in the reaction of peracetic acid with sabinene, we obtained two substances with smaller yields which, judging by their infrared spectra, do not contain a cyclopropane ring.

One of them—a compound of the composition $\text{C}_{10}\text{H}_{18}\text{O}_2$ (m.p. 143-144°), containing one hydroxy group but no carbonyl group, may be considered to have the structure of an epoxyalcohol (IV). The other substance, $\text{C}_{10}\text{H}_{16}$, is an unsaturated aldehyde. A special study will be devoted to the structure of these compounds.

EXPERIMENTAL

Preparation of sabinene. Sabinene was separated from the oily ester obtained from wild carrots (*Daucus carota* L.) grown in the Northern Caucasus (Zelenchukskii region).

B.p. 50 - 50.5° (15 mm), d_4^{20} 0.8496, n_D^{20} 1.4677, $[\alpha]_D - 84.03^\circ$.

Oxidation of sabinene by peracetic acid. The oxidation of sabinene (60 g) was carried out in dry ether by the gradual addition of an ether solution of peracetic acid containing 8.46 g of active oxygen, at a temperature of from -3 to +3°. On completion of the addition of the peracetic acid the reaction mixture was allowed to stand at room temperature. The oxidation was completed in 48 hours. The ether was driven off after washing the reaction product with a solution of soda and water and drying it over sodium sulfate. The remaining liquid was distilled in vacuo. The results of the distillation are shown in the table.

Investigation of the third fraction (sabineneglycol monoacetate). The third fraction was subjected to repeated distillation. 29 g sabineneglycol monoacetate was obtained.

B. p. 123-125° (5 mm), d_4^{20} 1.0352, n_D^{20} 1.4686, M_{rD} 57.03; calc. 57.13; $[\alpha]_D - 33.27^\circ$.

Found: C 68.22%, 67.92%; H 9.68%, 9.60%. Number of OH groups 1.13, 1.05; esterification number 262.9, 262.8. $\text{C}_{12}\text{H}_{20}\text{O}_3$, calculated C 67.89%, H 9.49%. Number of OH groups 1; esterification number 263.82.

Rotational dispersion: $[\alpha]_C - 28.0^\circ$, $[\alpha]_E - 44.6^\circ$, $[\alpha]_F - 55.0^\circ$, $\frac{[\alpha]_F}{[\alpha]_C} = 1.96$.

No. of fraction	Boiling point (8 mm)	n_D^{20}	n_D^{25}	d_4^{20}	Yield in g
1	68—70°	—30.08°	1.4710	0.9446	11.8
2	72—76	—49.52	1.4668	0.9443	4.8
3	124—127	—34.32	1.4683	1.0352	36.0

Saponification of sabineneglycol monoacetate. 20 g of the monoacetate was heated to boiling for one hour with a 0.5 N alcohol solution of caustic potash (250 ml). After distilling off the alcohol, the glycol was extracted with ether. The ether solution was washed with water and dried with sodium sulfate. After removing the ether, the residue was distilled in vacuo. The yield of sabineneglycol was 12 g (75%).

B.p. 135 - 136°. (6 mm), d_4^{20} 1.0228, n_D^{20} 1.4830, $M_R D$ 47.54; calculated 47.74; $[\alpha]_D -40.2^\circ$.

Found: C 70.28%, 70.36%; H 10.86%, 10.63%. Number of OH groups 1.95, 1.86. $C_{10}H_{18}O_2$. Calculated: C 70.54%, H 10.66%. Number of OH groups 2.

Rotational dispersion: $[\alpha]_C -30.6^\circ$, $[\alpha]_E -48.6^\circ$, $[\alpha]_F -57.6^\circ$.

Oxidation of sabineneglycol by lead tetraacetate. To 9.5 g of glycol dissolved in 100 ml of chloroform, small portions of a chloroform solution of lead tetraacetate [24.3 g Pb (OCOCH₃)₄ in 200 ml CHCl₃] were added with stirring. During the addition a 5 - 8° increase in temperature was noted. After all portions of the oxidizer were added, stirring was continued for one hour. Then the reaction mixture was left overnight. The oxidation reaction was complete in view of the fact that the quantity of lead diacetate (not soluble in chloroform) that separated out corresponded exactly to the calculated figure (16.5 g). The sabinaketone solution, after washing with a solution of soda and then with water, was dried over sodium sulfate. The yield of sabinaketone was 7.58 g (98%).

B.p. 89.5 - 90° (10 mm), d_4^{20} 0.9555, n_D^{20} 1.4682, $M_R D$ 40.22; calculated 40.08; $[\alpha]_D +22.4^\circ$. Data from literature [5]: b.p. 89° (10.5 mm), d_4^{25} 0.9510, n_D^{20} 1.4676, $[\alpha]_D -24.54^\circ$.

Found: C 78.20%, 77.98%; H 19.38%, 10.20%. $C_9H_{14}O$, calculated: C 78.21%, H 10.21%.

Investigation of the first fraction. On chilling the first fraction (see table), large crystals separated out (1.7 g). They were removed from the liquid by filtering in a Buchner funnel. After recrystallization from benzene their m.p. was 143 - 144°. Repeated crystallization showed no increase in the melting point.

Found: C 71.15%, 71.14%, H 10.85%, 10.84%. Number of OH groups 0.91, 1.12. $C_{10}H_{18}O_2$, calculated: C 70.54%, H 10.66%. Number of OH groups 1.

After removal of the crystalline material the liquid portion of the first fraction was distilled.

B.p. 74 - 76° (at 7 mm), d_4^{20} 0.9681, n_D^{20} 1.4710.

Found: C 78.66%, 78.77%; H 10.85%, 10.65%. $C_{10}H_{16}O$, calculated: C 78.89%, H 10.59%.

The substance $C_{10}H_{16}O$ does not contain a hydroxyl group. It tests positively for an aldehyde group (silver mirror) and for a double bond (reaction with tetranitromethane).

The infrared spectra were obtained by the aid of an IKS-12 spectrometer

SUMMARY

1. The main product obtained by the oxidation of sabinene by peracetic acid was sabineneglycol monoacetate. The liquid sabineneglycol formed by its saponification is apparently the stereoisomer of the sabineneglycol found by Semmler when he oxidized sabinene with potassium permanganate.

2. In addition to sabineneglycol monoacetate, the oxidation of sabinene yields two substances whose molecules do not contain a cyclopropane ring. One of these compounds is an epoxyalcohol whose composition is $C_{10}H_{18}O_2$ (m.p. 143 - 144°). The other is an unsaturated aldehyde whose composition is $C_{10}H_{16}O$.

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*Original Russian pagination. See C. B. translation.

THE CONDENSATION OF LUPININIC ACID WITH PIPERIDINE

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Willstatter, who carried out the oxidation of lupinine by chromic acid in a sulfuric acid solution, was the first to obtain lupininic acid with m.p. of 255°. The author, however, does not give the specific rotation of the acid he obtained. Subsequently Schopf repeated Willstatter's work and obtained the acid in the form of its methyl ester. In this way he succeeded in establishing the fact that, depending on conditions of oxidation, esters with different specific rotations ($[\alpha]_D$ from -19.4° to +5.8°) are formed. By saponification of the methyl ether of lupininic acid with $[\alpha]_D$ -10.4° the author obtained the hydrochloride of the acids with $[\alpha]_D$ -13.1°.

In view of the lack of detailed studies of lupininic acid, we decided to examine the oxidation products of lupinine by chromic acid more carefully, before proceeding to a study of the condensation reaction of the acid with piperidine.

We oxidized lupinine ($[\alpha]_D$ -21.7°) by Willstatter's method and found that a mixture of optical isomers of lupininic acid is formed, with the racemate predominating. By utilizing the differential solubility of the isomers in acetone, we separated from the mixture approximately 18% of the dextrorotatory isomer and 82% of the racemate.

d-Lupininic acid crystallizes from a mixture of acetone and water as glistening needles, m.p. 255°, $[\alpha]_D$ +55.2°. It is easily soluble in water, methanol, ethanol, slightly in chloroform, and is soluble in acetone and ether.

d,l-Lupininic acid crystallizes from dry acetone in grain-like form, m.p. 175°, $[\alpha]_D$ 0°. It is easily soluble in water, methanol, and ethanol, soluble in acetone only with difficulty and insoluble in ether.

A test mixture of d- and d,l-lupininic acids did not show a decrease in melting point. For a definitive confirmation of the identity of these acids we obtained their ethyl esters and found that a mixture of their picrates likewise failed to show a decrease in melting point.

The ethyl esters of d- and d,l-lupininic acids, described by us for the first time, have the following properties: the ester of d-lupininic acid - 125 - 130° (10 mm), $[\alpha]_D$ +45.5°, and the ester of d,l-lupininic acid - b.p. 130 - 140° (10 mm), $[\alpha]_D$ 0°.

The condensation of lupininic acids with piperidine was carried out by the direct reaction of the reagents in the presence of phosphorus pentoxide which yielded crystalline substances of the composition $C_{15}H_{26}ON_2$.

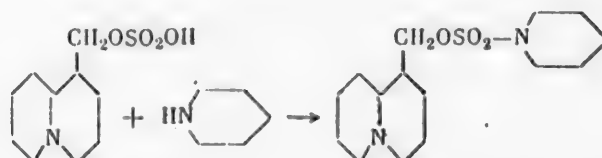


From d-lupinic acid a substance was obtained with m.p. 240 - 241°, $[\alpha]_D +18.7^\circ$. It is easily soluble in water and alcohol, but insoluble in acetone and ether.

d,l-Lupinic acid with piperidine gives two products, one with m.p. 180 - 182°, $[\alpha]_D 0^\circ$, and the other with m.p. 238 - 239° $[\alpha]_D +17.7^\circ$. The latter was identical with the substance obtained from the condensation of d-lupinic acid with piperidine.

The product with m.p. 180 - 182° does not differ in composition from the compound with m.p. 240 - 241° and there is no decrease in melting point when the two are mixed. From this we came to the conclusion that the substance with m.p. 180 - 182° is the racemate of the substance with m.p. 240 - 241°.

Incidentally we also studied the condensation reaction of the sulfuric acid ester of lupinine* with piperidine. We succeeded in separating out a compound of the composition $C_{15}H_{23}O_3N_2S$ with m.p. 108 - 110°, $[\alpha]_D -21.8^\circ$.



By saponifying this compound with 5% hydrochloric acid, a quantitative yield of sulfuric acid is obtained, as well as lupinine and piperidine.

EXPERIMENTAL

Lupinic acid. 100 g of lupinine ($[\alpha]_D -21.7^\circ$) and 17 ml of sulfuric acid were dissolved in 200 ml of water and mixed in the cold with 80 g of chromic anhydride and 66 ml of sulfuric acid (d 1.84) in 600 ml of water. The mixture heated up to 50 - 60° and after standing for an hour, the solution became green. After briefly boiling the solution, using a reflux condenser, an equal quantity of chromic anhydride and sulfuric acid was added to it and the mixture boiled for two hours. Excess chromic acid was reduced by passing sulfur dioxide through the solution after which sulfuric acid and chromium were precipitated by the addition of barium hydroxide. After filtering off the liquid, the precipitate was washed several times with hot water. The aqueous solution was evaporated to dryness and the residue was treated with anhydrous alcohol. After evaporating the alcohol 90 g (93.1%) of lupinic acid was obtained in the form of a thick gruel.

d- and d,l-Lupinic acids. To 10 g of technical lupinic acid were added 900 ml of acetone and 90 ml of water. The mixture was boiled on the water bath, with a reflux condenser, for 30 minutes. During this treatment the solution separated into layers—an acetone solution and a thick oil. The water-alcohol solution was separated from the oil by decantation, 900 ml of acetone (without water) were added to the oil and the mixture was boiled for 30 minutes. The acetone solution which was obtained was added to the water-acetone solution. The remaining oil, after being washed twice with acetone, solidified after standing in the cold. The solid product was subjected to recrystallization from a mixture of acetone and water, which was accomplished by suspending it in 200 ml of acetone, and while boiling it under a reflux condenser, adding water drop by drop to the suspension until the solid dissolved. Upon cooling the solution, glistening needle-like crystals of d-lupinic acid separated out, which, after being recrystallized twice from a mixture of acetone and water and being dried at 105°, had a m.p. of 255°. Yield 14.5 g. $[\alpha]_D +55.2^\circ$ (in alcohol).

Found: N 7.20%, 7.09%. $C_{10}H_{17}O_2N$. Calculated: N 7.6%.

From the water-acetone solution, after distillation of the acetone and evaporation to dryness, 70 g of d-lupinic acid were obtained. After repeated recrystallization from acetone this yielded crystals with m.p. 175°. $[\alpha]_D = 0^\circ$ (in alcohol).

Found: N 7.4%, 7.3%. $C_{10}H_{17}O_2N$. Calculated: N 7.6%.

* In the Department of Plant Chemistry of the Central Asian State University, one of us recently worked out a method of separating a mixture of anabasine and lupinine by means of sulfuric acid [3]. By using this method it is easily possible to separate lupinine as a free base or as a sulfuric acid ester.

The ethyl ester of d-lupinic acid. To 2.6 g of d-lupinic acid, with cooling, were added 13.5 ml of anhydrous alcohol and 5.4 ml of sulfuric acid (d 1.84). The mixture was heated on a water bath with a reflux condenser for two hours. The chilled product of the reaction was made alkaline by treatment with potash in the presence of ice and then was extracted with ether. After drying the ether solution over sodium sulfate and distilling off the ether, the residue was distilled in vacuo. B.p. 125-130° (10 mm). Yield 1.5 g (50.2%), $[\alpha]_D +45.5^\circ$ (in alcohol). It gave a crystalline picrate with m.p. 151-152° (from water).

Found: N 12.79%, 12.85%. $C_{12}H_{21}O_2N \cdot C_6H_2(NO_2)_3OH$, calculated: N 12.7%.

The ethyl ester of d-lupininic acid. The ester was obtained by the same procedure as in the case of the d-ester. From 2.6 g of d,l-lupininic acid 1.8 g of a complex ester with b.p. 130-140° (10 mm), $[\alpha]_D 0^\circ$ were obtained. Yield (60.2%).

The ester forms an oily picrate which, on triturating with water, forms a powder. After recrystallization from water its m.p. was 108-110°.

Found: N 12.42%, 12.55%. $C_{12}H_{21}O_2N \cdot C_6H_2(NO_2)_3OH$, calculated: N 12.7%.

Condensation of d-lupininic acid with piperidine. A mixture of 2 g of d-lupininic acid, 20 ml of piperidine and 7 g of phosphorus pentoxide was boiled under a reflux condenser for two hours. After cooling, the reaction mixture was made alkaline by treatment with potash, and then extracted first with ether and then with chloroform. The ether and chloroform extracts were dried over sodium sulfate and the solvents distilled off. The residue after removing the ether was unchanged piperidine; after removing the chloroform there remained crystals that were saturated with oil. Upon treatment with acetone the oil went into the acetone and the crystals became colorless. After repeated recrystallization from a mixture of ether and anhydrous alcohol the m.p. was 240-241°; $[\alpha]_D +18.7^\circ$ (in alcohol). Yield 1 g (37%).

Found: N 11.08%, 11.00%. $C_{15}H_{26}ON_2$, calculated: N 11.2%.

Condensation of d-lupininic acid with piperidine was carried out in the same way as in the preceding experiment. From 5 g of d-lupininic acid and 30 ml of piperidine, after treatment with acetone, 2.62 g (38.4%) of substance with m.p. of 180-182° (from a mixture of anhydrous alcohol and ether) were obtained; $[\alpha]_D 0^\circ$.

Found: N 11.09%, 10.95%. $C_{15}H_{26}ON_2$. Calculated: N 11.2%.

From the acetone mother solution on prolonged standing (several days) a white crystalline residue precipitate which, after recrystallization from a mixture of anhydrous alcohol and ether had a m.p. of 238-239°; $[\alpha]_D +17.7^\circ$. A mixture of this with the condensation product of d-lupininic acid and piperidine showed no increase in the melting point.

Condensation of the sulfuric acid ester of lupinine with piperidine. A mixture of 16 g of the sulfuric acid ester of lupinine ($[\alpha]_D -13.0^\circ$) and 35 ml of piperidine was boiled under a reflux condenser for 10 hours. After cooling and alkalinizing, the reaction products were extracted first with ether and then with chloroform. The ether yielded unchanged piperidine and the chloroform extract—after recrystallization from acetone—gave crystals with m.p. 108-110°; $[\alpha]_D -21.81^\circ$. Yield 17 g (83.7%).

Found: C 57.55%, 57.52%; H 9.50%, 9.02%; S 10.00%, 10.15%. $C_{15}H_{28}O_3N_2S$, calculated: C 57.00%, H 8.9%, S 10.1%.

A picrate with m.p. 215° (from alcohol) was formed.

Saponification of the condensation product. 0.6 g of the condensation product of the sulfuric acid ester of lupinine with piperidine was dissolved in 20 ml of 5% hydrochloric acid and heated for 10 hours. Sulfuric acid was separated from the reaction product by the addition of barium hydroxide (quantitatively). The barium sulfate was filtered off, washed with water, calcined and weighed. 0.4415 g of barium sulfate was obtained, which corresponds with one mole of sulfuric acid. The filtrate was saturated with potash and then extracted with ether. After drying over sodium sulfate and removal of ether, the residue began to crystallize (it had a strong smell of piperidine). Lupinine, purified by recrystallization from petroleum ether, has a m.p. of 68-69° C. Yield 0.27 g (63.0%). A mixture of this material with lupinine gave no depression of the melting point.

SUMMARY

- 1) The oxidation of lupinine by chromic acid was studied. For the first time it has been shown that along with d-lupininic acid, its racemate is also produced.
- 2) The ethyl ester of d-lupininic and d,l-lupininic acids were obtained and characterized.
- 3) The condensation of piperidine with d- and d,l-lupininic acids was studied. It was found that, under the given reaction conditions, the l-isomer of the condensation product was converted into the d-isomer.
- 4) The condensation of the sulfuric acid ester of lupinine with piperidine was carried out. The resulting complex ester was saponified and yielded the original substances.

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* Original Russian pagination. See C. B. translation.

LETTERS TO THE EDITOR

PECULIARITIES OF THE MASS SPECTRA OF ENYNE HYDROCARBONS CONTAINING A TERTIARY BUTYL RADICAL

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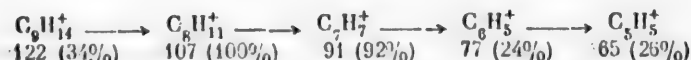
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 10,

pp. 3499-3500, October, 1960

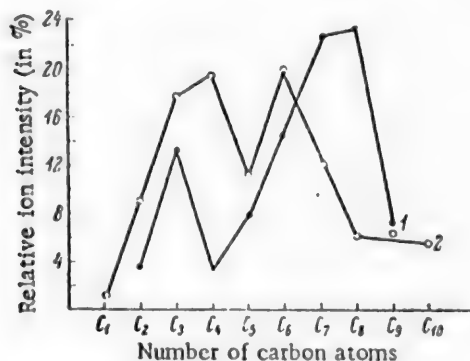
Original article submitted May 24, 1960

It has been shown previously that in the mass spectra of enyne hydrocarbons which do not contain tertiary butyl radicals, the ions $C_3H_3^+$ and $C_6H_6^+$ predominate [1]. A study of the enyne hydrocarbons containing tertiary butyl radicals — 2,5,5-trimethylhexene-1-yne-3 (I) and 2-tertiary butylhexene 1-yne-3 (II) — has shown that their dissociation proceeds in another manner.

For hydrocarbon (I), which contains a tertiary butyl radical at the triple bond, there is a successive splitting off of methyl groups with subsequent hydrogenation or dehydrogenation of the ions formed, according to the following scheme:

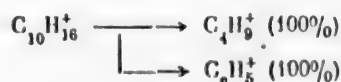


The disintegration of the ion $C_8H_{11}^+$ apparently includes processes of dehydrogenation and hydrogenation which lead to the formation of the thermodynamically stable fragment $C_7H_7^+$, which is possibly a tropyliene ion. The presence in the mass spectrum of a metastable ion of mass 76.6 confirms the correctness of such a disintegration mechanism.



Distribution of ions in mass spectra according to the number of carbon atoms.

Disintegration, with the splitting off of a tertiary butyl radical, is characteristic of hydrocarbon (II), during which a positive charge may, with equal probability, be found on either of the ions formed:



These peculiarities of enyne hydrocarbons with a tertiary butyl radical become evident in the distribution of ion intensities in accordance with the number of carbon atoms: the maximum on the curve for hydrocarbon (I) is displaced from $C_6H_6^+$ to $C_7H_7^+$ and $C_8H_8^+$; for hydrocarbon (II) it is displaced from $C_3H_3^+$ to $C_4H_4^+$ (see the figure, curves 1 and 2).

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- * Original Russian pagination. See C. B. translation.

THE REACTION OF α -CHLOROETHYLMETHYL ESTER WITH SODIUM ALKYL MALONIC ESTERS

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The reaction of α -chloroethylmethyl ester with sodium alkylmalonic esters has been little studied, although this ester, like other α -chloroethylmethyl esters appears to be an extremely reactive substance [1].

Alkyl- α -methoxyethylmalonic esters. $\text{CH}_3\text{CH}(\text{OCH}_3)\text{C}(\text{COOC}_2\text{H}_5)_2$

R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	MR _D		Found (%)		Empirical formula	Calc. (%)		Yield (%)
				found	calculated	C	H		C	H	
CH ₃	70-71° (0.5)	1.0324	1.4272	57.85	57.95	56.75	8.70	C ₁₁ H ₂₀ O ₄	56.90	8.62	60
C ₂ H ₅	77-78 (0.5)	1.0257	1.4332	62.36	62.57	58.36	8.97	C ₁₃ H ₂₂ O ₄	58.53	8.94	57
n-C ₄ H ₉	83-84 (0.5)	1.0122	1.4317	66.97	67.19	59.80	9.32	C ₁₅ H ₂₄ O ₄	59.97	9.29	52
iso-C ₄ H ₉	80-81 (0.5)	1.0184	1.4378	67.00	67.19	59.72	9.15	C ₁₅ H ₂₄ O ₄	59.97	9.29	48
CH(C ₆ H ₅) ₂	186-187° (0.5)	—	—	—	—	71.57	7.29	C ₂₃ H ₂₈ O ₄	71.87	7.29	78

M.p. 50-51° (from benzene).

The only work known is that of Renard and Dony [2], in which the reaction of α -chloroethylmethyl ester with malonic and ethylmalonic esters was studied. However, these authors did not carefully examine the substances they obtained since this reaction was not the principal object of their work.

We have studied the reaction of α -chloroethylmethyl ester with a series of sodium alkylmalonic esters in absolute ether, as a result of which we obtained the corresponding alkyl- α -methoxyethylmalonic esters whose properties are shown in the table.

Investigation of these esters is being continued.

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CATALYTIC DEHYDROCYCLIZATION OF TRIMETHYLHEXYLSILANE

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For the purpose of studying the possibility of dehydrocyclization of trimethylhexylsilane, we passed it over a chromium catalyst [1] at 530-590° and a volumetric flow rate of 30. It appeared that under these conditions, the dehydrocyclization of trimethylhexylsilane takes place with the formation of trimethylphenylsilane.



The aromatization of silicoparaffins appears to be a new reaction in silicoorganic chemistry. An intermediate product is an unsaturated silicohydrocarbon, the content of which in the condensates, determined by the method of thiocyanogenization, varied within the limits 7.5-21% (depending on temperature). Trimethylsilane, tetramethylsilane, pentenes, hexenes and benzene were found as byproducts.

The fraction with b.p. 163-165°, separated out by repeated distillation of the condensates, contains trimethylphenylsilane along with unchanged trimethylhexylsilane. Data from the literature for trimethylhexylsilane [2] are: b.p. 163°, n_D^{20} 1.4154; for trimethylphenylsilane [3]; b. p. 170-171°, n_D^{20} 1.4901.

The presence of trimethylphenylsilane in the fraction boiling at 163-165° is also confirmed, apart from the increase in the refractive index (n_D^{20} 1.4195), by spectrum analysis. The infrared spectrum obtained for this fraction has an absorption maximum characteristic of the phenyl nucleus linked to silicon (1117 and 1429 cm^{-1}) [4].

A search for more effective dehydrocyclization catalysts of silicoparaffins is being continued.

SUMMARY

The possibility of the catalytic dehydrocyclization of trimethylhexylsilane with the formation of trimethylphenylsilane has been demonstrated.

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NEW HYDROCARBONS OF THE CYCLOPROPANE SERIES

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Continuing our investigation of the chemistry of cyclopropanes [1, 2], we have succeeded in synthesizing several new hydrocarbons of this series.

1-Cyclopropylcyclohexadiene-1,4 and 1-methyl-4-cyclopropylcyclohexadiene-1,4 were obtained by the partial reduction of phenyl- and p-tolycyclopropane by sodium (in liquid ammonia) and methyl alcohol. Subsequent catalytic hydrogenation of the double bonds in 1-cyclopropylcyclohexadiene-1,4 (over a copper-chrome catalyst at 100 atm.) at 95° and then at 125° led to the formation of cyclopropylcyclohexene-1 and, correspondingly, of cyclopropylcyclohexane; the latter was also obtained by the methylenization [3] of vinylcyclohexane.

p-Cyclopropylstyrene and p-cyclopropylisopropenylbenzene were obtained by dehydration, respectively, of methyl- and dimethyl p-cyclopropylphenylcarbinol (both carbinols were obtained from p-cyclopropylacetophenone). p-Dicyclopropylbenzene was synthesized in two ways— from p-cyclopropylacetophenone by the series of reactions of Mannikh and Kizhner [4], and from p-cyclopropylstyrene by methylenization [3].

The constants of all the hydrocarbons we synthesized that contain three-membered rings are shown in the table.

Hydrocarbon	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	$M R_p$	
				found	calculated
1-Cyclopropylcyclohexadiene-1,4	179° (732)	1.5035	0.9170	39.31	39.14
1-Methyl-4-cyclopropylcyclohexadiene-1,4	197 (750)	1.5000	0.9079	44.20	43.76
Cyclopropylcyclohexene-1	168.3 (747)	1.4865	0.8845	39.71	39.60
Cyclopropylcyclohexene-1 from cyclopropylcyclohexene-1	157.5—158 (747)	1.4560	0.8368	40.31	40.07
	157.3 (746)	1.4535	0.8393	40.01	40.07
p-Cyclopropylstyrene	105—106 (12)	1.5632	0.9628	48.65	47.44
p-Cyclopropylisopropenylbenzene	123 (14)	1.5630	0.9515	54.00	52.06
p-Dicyclopropylbenzene: from p-cyclopropylacetophenone from p-cyclopropylstyrene	211 (755)	1.5340	0.9472	51.94	51.04
	82—83 (2)	1.5343	0.9468	51.98	51.04

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THE REACTION OF DICHLOROCARBENE WITH ENYNE HYDROCARBONS

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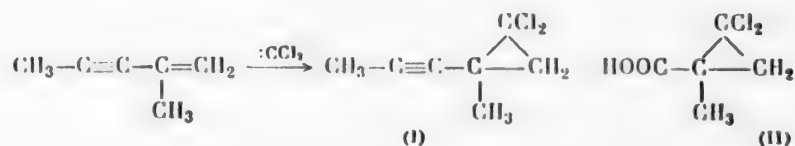
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The present letter describes reaction between dichlorocarbene and enyne hydrocarbons—2-methylpentene-1-yne-3 and 2-methylhexene-2-yne-4.

Taking into consideration the electrophilic character of dichlorocarbene [1], a more or less selective linking to the double bond of the enyne system was to be expected. This assumption was confirmed by experiment in the case of 2-methylpentene-1-yne-3. The dichloride (I) was the only product isolated from the reaction.



In contrast to the majority of other work relating to this field, dichlorocarbene was obtained by the thermolysis of sodium trichloroacetate in a solution of 1,2-dimethoxyethane. 26 g (0.325 moles) of hydrocarbon, 26 g (0.140 moles) of sodium trichloroacetate and 30 g of 1,2-dimethoxyethane were heated at 100° with mechanical stirring for seven hours in an atmosphere of nitrogen. On completion of the reaction a precipitate of NaCl was filtered off and the reaction product was distilled in vacuo. Yield (I) 4.5 g (20% of that calculated on the basis of the trichloroacetate used).

B.p. 61° (10 mm), n_D^{20} 1.4906, D_4^{20} 1.1432.

Found: C 51.76%, 51.72%; H. 5.47%, 5.42%; Cl 43.76%, 43.28%. $\text{C}_7\text{H}_5\text{Cl}_2$, calculated: C 51.57%; H 4.91% Cl 43.53%.

Infrared spectrum: 757 (v.s.), 1028 (s), 1384 (s), 1450 (v.s.), 2252 (med.).

The band corresponding to the valence vibration of the C=C bond (I) is absent from the infrared spectrum.

By oxidizing (I) with a solution of KMnO_4 in acetone in the presence of sodium bicarbonate, the acid already known in the literature with m.p. 60-61° (from petroleum ether) was obtained. From the literature: m.p. 60-62° [2].

Found: Cl 41.96%. $\text{C}_6\text{H}_5\text{Cl}_2$, calculated: Cl 42.0%

The result of the oxidation confirms the structure (I). In this example the possibility of the selective linking of dichlorocarbene to a double bond of an enyne hydrocarbon was demonstrated. However in the case of the reaction of dichlorocarbene with 2-methylhexene-2-yne-4, the selective linking to the double bond was not observed. As a result of the reaction of dichlorocarbene with 2-methylhexene-2-yne-4, under the conditions mentioned above, we obtained a mixture of chlorides with a 20% yield.

B. p. 28-35° (0.1 mm). Found: Cl 39.2%. $C_3H_4Cl_2$, calculated: Cl 40.04%.

Some decrease in the content of chlorine, apparently, may be explained by the slight hydrolyzability of one of the components of the mixture. As a matter of fact, by reacting with a 5% soda solution at 60°, approximately 30-40% of the chloride is hydrolyzed. As is well known, 1,1-haloidecyclopropanes cannot be hydrolyzed under these conditions [3]. The infrared spectrum of the reaction products also pointed to the fact that we were dealing with a mixture of chlorides, since the frequencies for both double and triple bonds were present.

In this research, the reaction between dichlorocarbene and enyne hydrocarbons was accomplished for the first time.

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A NEW METHOD FOR THE SYNTHESIS OF p-TERPHENYLS

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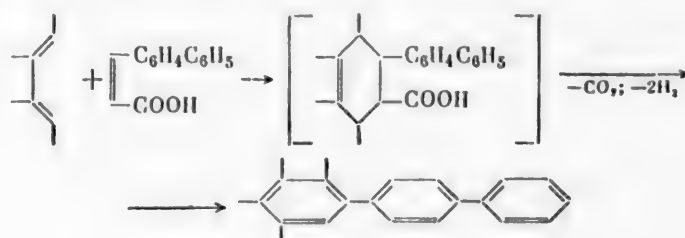
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In studying the diene synthesis between *n*-phenylcinnamic acid and various diene hydrocarbons, we found conditions (16 - 18 hour heating at 300° of a benzene solution of *p*-phenylcinnamic acid with a double excess of alkadiene in a steel autoclave without a bearing, in the presence of 0.1 g of picric acid and 0.1 g of hydroquinone), under which the addition products formed—2-*p*-diphenyl-1,2,3,6-tetrahydrobenzoic acids—are immediately decarboxylated and dehydrogenated with the formation of *p*-terphenyls.



p-Terphenyls from *p*-Phenylcinnamic Acid and Alkadienes

No.	Names	Starting Alkadiene	Yield in %	Melting point	Ultraviolet spectra	
					λ_{\max}	$\lg \epsilon_{\max}$
(I)	<i>p</i> -Terphenyl	Divinyl	48	209.5 - 210°	280	4.41
(II)	3-Methyl- <i>p</i> -terphenyl	Piperylene	55	126 - 127	291	4.54
(III)	4-Methyl- <i>p</i> -terphenyl	Isoprene	55	207	285	4.64
(IV)	3,4-Dimethyl- <i>p</i> -terphenyl	2,3-Dimethylbutadiene-1,3	55	127	285	4.53
					362	2.18
					382	1.85

The *p*-terphenyls (I - IV) (see the table) were separated by distilling the reaction mixture in vacuo (2 - 3 mm) and were purified by recrystallization from alcohol (I - III) or from acetonitrile (IV) and sublimation in vacuo.

